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Feb. 1908

MANUAL

OF

ANTENATAL PATHOLOGY

AND HYGIENE

THE EMBRYO

BY

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PREFACE

THE companion volume to this, which appeared in 1902, dealt specially with the diseases of the fœtus; this is concerned with the pathology of the embryo, and, to a small extent, with the morbid tendencies of the germ. The two volumes are intended to give the reader an idea of the whole extent and variety of the pathological processes of antenatal life.

The pathology of the embryo is practically synonymous with the subject of Teratology, or at least with that part of it which deals with single as distinguished from double monsters. Now, Teratology may be studied in three different ways: a simple description may be given of the various monstrosities, with regard to their anatomy, physiology, social and economic results, and the like; or teratological phenomena may be used for the purpose of explaining embryological problems or as a means of clearing up difficulties in the domain of fœtal physiology; or, finally, the whole subject may be approached from the side of causation, and attention be focused upon the genetic aspects of abnormal formations. While not neglecting the first and second methods of study, I have endeavoured to specialise the third plan; for, after all, the most important matter is to reach a solution of the problem of causation, because, if that be reached, there begins to be hope that preventive treatment may be discovered. In my opinion, therefore, Chapters VII. to XII., which discuss teratogenesis on general principles, are the most important of all.

The greater part of this volume, then, is given to the consideration of the pathology of the embryo, and only three chapters at the end are set aside for the pathology of the germinal period of life. This fact requires a word or two of explanation. I had originally intended to treat the pathology of the germ, which may, roughly speaking, be regarded as synonymous with double monsters and morbid heredity, on the same scale of completeness as that of the fœtus and embryo; but this, I soon found, would have entailed the writing of a third volume not much smaller in size than the present.

For such a task I have not the time, even if I have the ability, which I doubt. I determined, therefore, simply to present in Chapters XXXI., XXXII., and XXXIII. a very brief sketch of the plan I had drawn out for the treatment of this division of the whole subject. If it do no more, it will serve to give an idea of the morbid processes which may be believed to be initiated or determined in germinal life. The importance of these may be estimated when it is said that I believe that they include the double monsters (both symmetrical and asymmetrical), most neoplasms, plural births, and the mysterious phenomena of morbid heredity. I wish, however, to emphasise the fact that I am giving only a sketch and not a fully filled-in picture of this important section of antenatal pathology.

I have paid special attention to the bibliographical notices and references, and, as in the first volume, I have tried as far as possible to give the reader references which themselves contain literature lists. I have endeavoured to verify all these, and to give for each the volume, the page, and the year of publication; this has been a task of great magnitude, and unaided I should have been forced to abandon it, but, with the help of the *Index Catalogue* of Washington, the *Index Medicus*, and Taruffi's fine work (*Storia della teratologia*) in eight volumes, it has been accomplished. The reader will never know how many inaccurate references have been corrected, and how many weary hours have been spent in putting right the errors which greater care on the part of earlier writers would have prevented. Here is a single example and a glaring one. In Taruffi's *Storia* (vol. vi. p. 149) I found a reference to the case of a woman who had given birth to six anencephalic fœtuses; it was *Adam Mencer, A. Medical Times and Gazette, Dicem.* 1861. I looked up this reference and could find no trace of it; I looked up the indexes of adjacent volumes and fared no better. I then thought that perhaps *Mercer Adam* was meant, and I referred to his articles on Teratology in the *Edinburgh and London Monthly Journal of Medical Science*, and there, in his second article, I found it, not the case indeed, but a reference back to one reported by J. Martin in the *New York Journal of Medicine* for March 1849. Then, as it happened, the only set of this Journal to which I could gain access lacked the very volume I wanted. Then I went to the *Index Catalogue* and found that J. Martin's paper had also appeared in the *Medical Examiner* of Philadelphia for 1849; I looked up this and got the original reference at last. So Taruffi's *Adam Mencer, A. Medical Times and Gazette, Dicem.* 1861, had become *Martin, J., Med. Exam. Phila.*, 1849, n.s., v. 23!

I may take this opportunity of thanking the Committee and

Council of the Royal College of Physicians, Edinburgh, who granted me, in 1902, one half of the Cullen Prize, in recognition of my work on Antenatal Pathology.

I have again to thank my friend Dr. JOHN THOMSON for the care and trouble which he has taken with the revision of the proof sheets, as well as for the suggestions which he has from time to time made, and always for the benefit of the work. It is also a pleasure to me to express my gratitude to the many medical men who have placed specimens at my disposal which have made my study of the subject a possibility. A list of these will be found in the Appendix.

J. W. BALLANTYNE.

24 MELVILLE STREET, EDINBURGH,
September 16, 1904.

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MANUAL OF ANTENATAL PATHOLOGY AND HYGIENE

BOOK III

THE PATHOLOGY OF THE EMBRYO

CHAPTER I

Divisions of Antenatal Life; Embryonic Period; Contrast between Fœtal and Embryonic Physiology; Functions of Organs and Formation of Organs; Contrast between Fœtal and Embryonic Pathology; Nosography and Teratology; Necessity for the Preliminary Study of Embryology.

Divisions of Antenatal Life.

As was pointed out in the first chapter of the first section of this work (Manual of Antenatal Pathology and Hygiene—The Fœtus, p. 7, 1902), antenatal life may be divided into three periods—the fœtal, the embryonic, and the germinal. These periods differ considerably in length: the fœtal occupies thirty-two weeks of intrauterine life, or thirty-four if the short neofœtal period be included; the embryonic, five weeks, or seven if the neofœtal period be reckoned with it; while the germinal period stretches back almost indefinitely into the lives of parents and earlier ancestors, if the theory of the continuity of the germ-plasm be accepted.

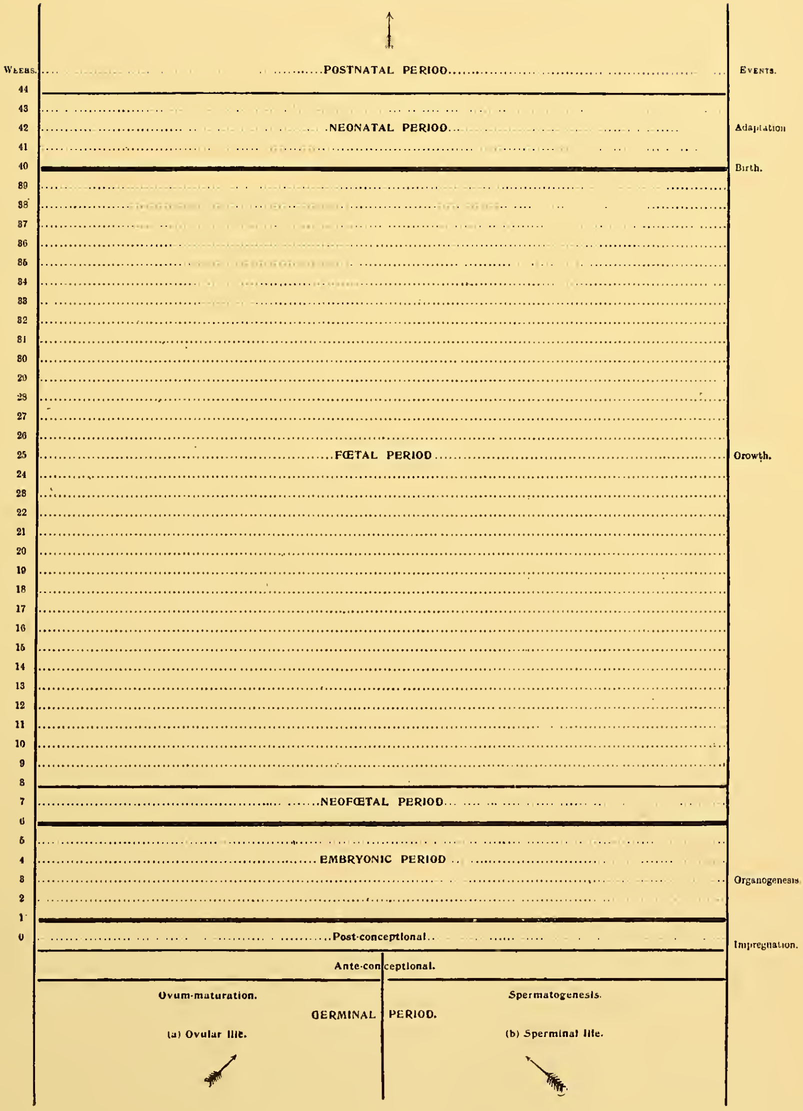
The greater part of intrauterine life is fœtal, and the smaller part is embryonic. It has sometimes been stated that the earliest part of embryonic life is in progress while the blastodermic vesicle is still in the Fallopian tube; but there seems to be good evidence to show that during the whole of these two periods (fœtal and embryonic) the new organism is inside the body of the uterus, save only in the pathological condition of extrauterine pregnancy when development takes place wholly or in part in the interior of the Fallopian tube. It is doubtful whether any part of germinal life is carried on in utero. This period ends with the appearance of the first traces of the embryo in the embryonic area of the blastodermic vesicle; and, if it be believed that impregnation and the first stages of development occur in the Fallopian tube, then it is quite likely that no part of germinal life is enacted in the cavity of the uterus. Whether this be so or not, there can be no doubt that by far the greatest part of the germinal period of existence takes place in the sexual glands of the parents, where the ova and spermatozoa lie quiescent but probably capable of being impressed by chemical and other changes occurring in their immediate neighbourhood. These matters will be more clearly understood with the help of the scheme of the divisions of antenatal life on page 3 (Fig. 1).

It was also pointed out in the first section of this work that each period of antenatal life had to a large extent a pathology peculiar to itself; it was stated that morbid causes acting upon the organism in the fœtal period produced results different from those arising in the embryonic period or in the germinal, although all the while the morbid causes might be the same. There was, therefore, a pathology of the fœtus, a pathology of the embryo, and a pathology of the germ. In the first section of this MANUAL the pathology of the fœtus was fully dealt with, while those of the embryo and germ were merely referred to incidentally when either happened to throw light upon or to be associated with truly fœtal morbid processes. In this, the second section of the work, it is the pathology of the embryo that calls for special consideration, while merely passing references will be made to that of the fœtus. Further, an attempt will be made to separate the pathology of the embryo from that of the germ, although it must be frankly confessed that such a separation is at present largely a matter of conjecture. This volume, then, is occupied with the *pathology of the embryo.*

As with the fœtus so with the embryo, it will be found most convenient to make the consideration and description of its anatomy and physiology precede the study of its pathology. When great differences exist between the physiological conditions of two epochs of life, great differences will also be noted in their pathological manifestations. At any rate, the physiology of the fœtus has been shown to have a far-reaching effect upon its pathology—to penetrate it through and through (*durch und durch durchdringen*) to use Graetzer's expressive phrase (*Die Krankheiten des Fœtus*, p. 3, 1837); and it may be expected that the physiological characters of embryonic life will leave their impress upon the morbid conditions then arising. As a matter of fact, a more complete and striking difference could scarcely be imagined than that which exists between the results of pathological activity in the fœtus and in the embryo: in the one case diseases are met with, which, while they present certain features which are peculiar, are yet evidently of the same nature as the maladies of postnatal life; in the other case, the morbid conditions found are so extraordinarily dissimilar from anything else in the whole field of pathology as to suggest that an altogether special cause has been at work in their production. Yet, if our generalisa-

FIG. 1.

THE DIVISIONS OF ANTENATAL LIFE.



tion be correct, the explanation of this dissimilarity may be contained in the existence of great differences between the physiological conditions of these two periods of antenatal existence. Is then the physiology of embryonic life strikingly unlike that of fœtal life? Let us see.

The Contrast between Fœtal and Embryonic Physiology.

The fœtus, in its physiology, shows resemblances of a real kind to the child at birth and to the adult. It is true that these resemblances are in some measure obscured by the dissimilar surroundings in which fœtal, as contrasted with postnatal, life is carried on; nevertheless in the unborn infant as in the child or adult there is the picture of a congeries of organs regularly performing their functions of circulation, digestion, assimilation, excretion, and the like. There are organs, and these organs are functionally active. In the fœtus some of the organs are less active and some doubtless are more active than in the child or adult; some also are active in somewhat different ways; yet the essential resemblance is maintained. The presence of an additional organ, the placenta, in the case of the fœtus, and the peculiarities of an intrauterine life, give to fœtal physiology a character peculiarly its own, but do not destroy the likeness which it bears to postnatal physiology. The only circumstance which tends seriously to mask the resemblance between the functions of the unborn and those of the new-born infant is the presence of developmental processes in the former. Some of the organs of the fœtus can hardly be described as performing functions or at any rate as performing nothing but functions, for they are still themselves in process of being formed. To express this fact in perhaps a more accurate way, some of the fœtal organs, such as the brain, are still occupied with the great function of development and are not sufficiently elaborated to have any other functions. In this respect certainly the physiology of the fœtus stands somewhat apart from the physiology of postnatal existence; in this one character there is a real difference between the functional activities of these two periods of life. But the difference is not great enough to prevent the observer from recognising in the fœtus the same kind of physiological activity as is seen in the infant, child, or adult. Let us turn now to the physiology of the embryo.

The physiology of the embryo is embryology: what is embraced by the name Embryology is really almost the only function, if it can so be called, of embryonic life. To gain a clear idea of embryonic physiology it is necessary to think not of organs performing functions but of organs being formed; embryonic physiology has not to do with organs and their special activities, but with the special activity which produces, builds up, and perfects the organs themselves. The great, almost the only, function of the embryo is to form tissues and organs, or, in one word, *organogenesis*. We have to imagine an aggregate of cells arranging themselves, apparently in a disorderly fashion or in a fashion of which the order is but dimly discerned, first into the three layers of the blastoderm, and then, after many intermediate stages and phases, into the organs which take on the particular functions of fœtal and postnatal life. There is no anatomy of the embryo apart from its physiology; the two are united together in the subject of embryology, which, as it were, contains them. It is only in fœtal life that the distinction between matters anatomical and matters physiological begins to become apparent; after birth it is, of course, quite evident. For the sake of strict accuracy, however, it must be added that the later part of embryonic life is not without indications of functional activity (in the ordinary sense of the term), and some of the organs, *e.g.* the heart, are performing other acts than those of formation or construction merely. In a similar manner the early part of fœtal life shows signs of constructive and formative activity in certain organs which have hardly yet begun to be operative in a functional way. There is, therefore, no sharply marked boundary between fœtal and embryonic life in this respect. The experienced biologist ought not, on reflection, to look for it. There is rather a gradual passage from the typical embryonic life of organogenesis to the typical fœtal life of growth and functional activity through a series of intermediate phases in which one or the other of these forms of vital action seems to preponderate. These intermediate phases were to be expected, Nature in her operations making no sudden transitions. At the same time, and after due allowance has been made for these connecting links, it can be recognised that the principal manifestation of embryonic life stands out prominently as organogenesis, while the chief sign of fœtal life is the functional activity of the various organs which go to constitute the fœtal economy.

Contrast between Fœtal and Embryonic Pathology.

The statements which have been made in the preceding paragraph abundantly prove that there is a fundamental dissimilarity between the physiology of the fœtus and that of the embryo. It is indeed scarcely possible to imagine two forms of vital activity less alike. We can now return with less surprise to the statement that the pathology of the embryo is startlingly unlike that of the fœtus. With a physiology so special, there is little room for wonder if the pathology also be of its own kind. In fact, one is led to look for morbid processes of a peculiar kind under circumstances which are so peculiar. There is here a conjunction of conditions which may be reasonably expected to produce something *sui generis*, something quite unlike what happens at any other period of life, postnatal or antenatal.

To state the matter concisely, the pathology of the embryo is Teratology. Since the chief result of the physiological activity of the embryo is the formation of parts and organs, so the chief result of pathological processes in the embryo is the malformation of its parts and organs. The one leads to normal formation, the other to abnormal formation. Monstrosities and structural anomalies are the results of morbid agents acting upon the organism in the embryonic period of its existence, or, to write more exactly, upon such parts of the organism as are in the embryonic or formative stage. It will be afterwards shown that there is good reason to believe that the morbid agents or causes are in no way peculiar in the embryonic epoch, and proof will be led that they are in fact just the same causes which produce diseases by their action upon the fœtal or adult organism. In the case of the embryo they are called teratogenic and in that of the fœtus or adult they are named pathogenic; but there is no sufficient reason for supposing that in their essential nature they differ one whit. It is the result which is dissimilar, being in the one instance teratological and in the other pathological. The mode of action of the cause is no doubt different, and the organism upon which it acts and its surroundings are indeed widely different; it is in this manner that the vast difference between the results—a monstrosity and a disease—is produced. The difference then between teratogenesis and pathogenesis is one of results rather than of causes; this I hope to make clear in the following chapters.

The pathology of the embryo, then, has to do with monstrosities and malformations, with, in other words, the teratological states. At the same time all that is teratological does not of necessity belong to the embryonic period, neither are all the manifestations of pathological activity in the embryonic period of necessity teratological. It has, for instance, been shown (in the first section of this work) that some malformations may arise in the fœtal period of antenatal life; these are the structural anomalies of such parts as the brain, genital organs, and skeleton whose development has continued after the termination of the embryonic period properly so called. Again, united twins are instances of teratological states which in all probability are determined in the germinal period of antenatal life. Further, some of the organs and parts of the embryo are so far advanced in formation before the end of the embryonic period as to be capable of some degree of functional activity, and they may therefore become the possible seats of disease; but this is a matter about which little is known, and it is hardly wise to speculate concerning it. These exceptions, however, do not greatly weaken the generalisation which has just been made, namely, that the pathology of the embryo is Teratology. Without doubt, the most numerous and the most characteristic of the morbid states which arise in embryonic life are teratological in their nature. The description of the morbid states of the fœtus forms part of Nosography, for these states are mainly of the nature of diseases; the description of the morbid states of the embryo, on the other hand, is Teratology, for they are chiefly of the nature of malformations and monstrosities.

I have endeavoured to place clearly before the reader the contrast between fœtal pathology and embryonic pathology, between Nosography and Teratology. I regard it as a fundamental and essential difference, as a distinction which must be rightly appreciated and constantly borne in mind if the phenomena of pathological activity in the embryo are to be properly understood.

Necessity for the Preliminary Study of Embryology.

In order that the manifestations of disturbed developmental processes may be recognised and their mode of production made intelligible, it is obvious that there must be a preliminary acquaintance with the phenomena and laws of normal development. Embryology has to do with the study of the normal development of the embryo, just as Teratology has to do with the study of its abnormal development. A knowledge of Embryology must precede the investigation of Teratology, if that investigation is to be fruitful in results of scientific value. The following five chapters will, therefore, be occupied with a short sketch of Human Embryology; thereafter it will be at least a little less difficult to unravel some of the many tangled problems of Teratology. Unfortunately it is not yet possible to set forth with accuracy of detail the various changes which occur in embryonic organogenesis; about many of them the information obtainable is fragmentary and uncertain, and about some of them there is no information at all. Human Embryology is an incomplete narrative; a great part of the first volume is wanting and has to be supplied by conjecture, and there are pages amissing throughout the rest of the work. We have to supplement our information about human Embryology by facts borrowed from Comparative Embryology, and we can hardly take it for granted that what happens in the chick will happen also in the human embryo. Since, then, we do not possess a complete knowledge of the anatomy and physiology of the embryo —Embryology, we cannot hope to explain with certainty all the processes concerned with pathology of the embryo—Teratology. At the same time it is by no means necessary to suspend investigations into the causation of monstrosities and malformations on account of this lack of accurate information regarding many parts of Embryology. Indeed the inquiry into several types of malformation and structural anomaly has repeatedly thrown light not only upon the malformation or anomaly itself but also upon the normal process of development the disturbance of which it represents. No surprise need be felt that this result has followed; for has not the investigation of the action of various organs in disease cleared up matters which were obscure regarding the functions of these organs in health? Physiology and pathology are mutually serviceable in explaining each other.

CHAPTER II

Embryology, the Anatomy and Physiology of the Embryo; Definition; General Principles of the Subject: Progress towards the Complex and Special; Varieties of Heterogeneity; Mechanism of Organogenetic Alterations and Evolutions; the Specificness of Ontogenesis; the Increase in Embryological Complexity in the higher Animal Forms; the Principle of "Recapitulation," Definition, Description, and possible Exceptions; Anisotropy and Isotropy.

Embryology, if the word be used in a restricted sense, is the science which treats of the origin and formation of the parts and organs of the embryo. It is the study of the anatomy and physiology of embryonic life; for it has to do with the description of the parts which make up the embryo or its *anatomy*, as well as with the way in which these parts, often after passing through several intermediate forms, become the permanent organs of the embryo, or its *physiology*. It is not possible to separate the anatomical from the physiological part of the subject. It is quite possible, and indeed it is easy, to describe the organs and parts of the adult body, *e.g.* the individual bones of the skeleton, without referring to their functions, for they are fully formed and do not differ save in size at the various periods of life. To attempt, however, to describe the parts of the embryo is really to picture these parts as they appear at the various stages in the development of the embryo, in other words it is to represent their progressive elaboration. When an embryologist speaks of, say, the face of the human embryo, he is thinking of the five processes springing from the base of the primitive cerebral capsule, and gradually growing round the cavity of the stomodœum, and ultimately uniting to form the facial framework; a living picture is as it were passing before his mind's eye. Embryology is, or ought to be, a kinematographic representation, a lifelike reproduction of the original moving scene of the whole embryonic period of antenatal existence. The embryo is not like a finished piece of machinery which can be studied both in action and at rest; it is unfinished, it is like a piece of machinery in process of construction, and its activities consist in a ceaseless progress towards a termination which shall be also a completion. In one sense (a limited one) the human embryo attains this finished stage with the close of the embryonic period of antenatal life; but in another sense (a wider one) it has not reached it even at the moment of birth, for some construction or organogenesis goes on postnatally. In another and yet wider sense it may be said of the human embryo that evolution has not brought it even now to full fruition, and that the world has not yet beheld the final phase in the ascent of man in the production of the embryo perfect in every part and without dangerous structural relics and morbid tendencies. It may never be brought so far, but Hope whispers that it may approach a little nearer than now.

> "Tutto che questa gente maledetta
> In vera perfezion giammai non vada,
> Di là, più che di qua, essere aspetta."[1]

In a more usual and less restricted sense Embryology is the science which treats of all the vital phenomena which occur in the uterus and ovary before birth; in this sense, therefore, it includes fœtal physiology and germinal activity as well as ovulation and even menstruation. Its employment, however, in this extended sense is not to be commended. It is but one instance, although a very prominent one, of the general looseness of definition which has prevailed regarding the terminology of antenatal affairs; for instance, the name embryo has been applied to the new organism in the uterus both in the fœtal and in the embryonic period, while to the word fœtus the same wide significance has been given; again, to cite a still more evident example, the term ovum has been used not only for the female sexual cell both before and after impregnation, but also for the product of conception at the various months of intra-uterine life. Such a usage of terms is sadly lacking in scientific accuracy. In this work the word Embryology is employed as meaning the science which treats of the origin and formation of the parts and organs of the embryo;[2] it deals with a part of antenatal existence which, although somewhat short (five to seven weeks), is so crowded with events of such importance as to cause it to take rank above all the other periods of life, antenatal and postnatal. It includes the study of all the changes through which the embryo passes, from the appearance of its first rudiments in the embryonic area up to the transformation of the "transition organism" into the recognisably-human embryo or neofœtus, as has been sketched in the first section of this work (MANUAL OF ANTENATAL PATHOLOGY AND HYGIENE, p. 80, 1902).

General Principles of Embryology.

The general principles of Embryology lie buried somewhat deeply; they are far from the surface, and not easily to be reached or recognised when reached. It is difficult for the mind to picture a stage in the life of the organism when almost the only manifestation of vital activity is of the purely constructive kind, when, in other words, the framework of the body is being built up. So complex also is the process that certain portions of it, notwithstanding the laborious researches of keen and able embryologists, are still imperfectly understood or only guessed at. It is even more difficult to discover the laws which govern embryological processes, and to trace the general principles which underlie so complex a series of manifestations. One is almost driven to speculate whether, after all, there are laws regulating the mysterious metamorphoses of the embryo, whether indeed the parts do not fall together in kaleidoscopic fashion, and confusion happen somehow to give place to order. But reflection assures the investigator that there must be laws, otherwise he is forced to state that Embryology differs from all the other sciences in being uncontrolled by rule. Yet in no other part of biological study is it so difficult to trace and analyse the laws and their results. Events move so rapidly, form succeeds form and phase follows phase with such swiftness and with so much partial superposition, that nothing less than an arrestment of the succession of phenomena at various stages would serve to enable the embryologist to trace the procession of occurrences. Such an arrestment sometimes occurs, and pathology comes to our aid to help us to understand the intricacies of physiology; but the arrestment is usually of a local and incomplete kind, and its immediate effect is too often simply to increase the complexity of the problem we are attempting to solve. At the same time progress has been made, and further progress will yet be made by means of the careful study of these partial arrestments, which we may at once call teratological phenomena, and so ultimately the abnormal and the normal will prove mutually elucidative. In what remains of this chapter it is my purpose to try to educe from the embryological and teratological data at command such general principles and laws as may seem to be educible. Let the reader meanwhile bear in mind that some of these principles rest upon very insecure foundations, and that after all there is but little advantage in formulating statements which are apparently definite, concise, and clear-cut if the facts do not warrant them or if the facts are not sufficiently known to warrant them. Facts must not be twisted to suit general principles, but general principles must be allowed slowly and surely to emerge from the rigorous investigation and comparison of facts. The principles which follow may be said to be emerging from the crucible of modern exact research; they are not all pure gold, but they have appreciably been cleansed from some impurities.

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[1] Dante, *Divina Commedia*, *Inferno*, vi. 109 :—

"Though ne'er to true perfection may arrive
This race accurs'd, yet nearer then than now
They shall approach it."
(*Cary's Transl.*)

[2] The word *Embryography* might, perhaps, be used in this sense; but the writer does not desire to complicate matters by the introduction of many terms.

First, it may be stated with a large degree of confidence that the main progress of events and changes in Embryology is from the simple towards the complex and from the general towards the special; there is a trend towards elaboration, and from a homogeneity which is at any rate apparent even if it be not real there arises a heterogeneity which is both evident and real. From the comparatively simple-looking impregnated ovum comes the superlatively complicated embryo. From the successive divisions of that wonderful unicellular organism come all the tissues and organs of the still more wonderful multicellular organism. To the series of changes which are thus induced and in which we see the constant trend towards an increasing complexity the name *ontogenesis* has been given. It has, it is true, been employed in a somewhat wider sense ("the origin and development of the individual living being"), but it will be convenient to use it here as indicating the changes in the impregnated ovum by which it becomes a fully formed embryo. As this progressive differentiation is going on, generation after generation of cells comes forward and plays its part, being always represented by a yet more numerous progeny of cells, and so ontogenesis may be regarded as a great genealogical tree (Delage[1]). In this genealogical tree, however, the successive generations do not coexist, but one gives place to the next and is indeed represented by it, for its cells have divided to form it.

Second, the heterogeneity which is produced in the process of ontogenesis is of two kinds. In one of these the differences are seen in the cells themselves; they grow unlike one another; there is a histological differentiation. In the other the differences are visible in the arrangement of the cells into organs; they are built together in different ways into organs; there is an organogenetic differentiation. There are different sorts of cells, and they are arranged in different sorts of ways.

Third, the startlingly divergent results found in the organs of the fully formed embryo may probably all be ascribed to differences in the rate of growth of the tissues composing the various organs and parts. In this way the manifold twistings and overlappings and separations and approximations which are seen in all embryos before their parts settle down into their permanent relationships are to be accounted for. A greater rapidity of growth of one part will cause a projection outwards or inwards at that part; a slowly growing part will find itself surrounded, built in, so to say, by the more active neighbouring areas; two organs at first far from each other may come into contact if both grow at a quicker rate than the body as a whole, they may even do so if one only grows faster, but then the meeting-place will not be the same. We speak in a loose fashion of the movement of various parts of the embryo in development, but the idea conveyed is erroneous if we mean by it that one organ without altering its rate of growth approaches another or passes away from it.

Fourth, there is a specificness in the ontogenesis of different types of animals. The embryos of different animals do not travel by the same route to reach their later stages; there is a wide diversity between their ontogenetic processes, how wide we do not probably fully realise as yet. Even when the fully formed organ or part in two species of embryo seems to be exactly similar, it does not apparently follow that it has reached this state by the same series of alterations. The embryo of the chick differs from that of the mammal in the details of its development; further, each has an amnion, but there is good reason to believe that it is not formed in the same manner in each. This principle cannot be too clearly kept in mind; for in the past it has been neglected, and what was observed in the chick embryo was regarded as proven also for the human embryo, with results which were disastrous so far as accuracy was concerned.

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[1] Delage, Y., *La structure du protoplasme et les théories sur l'hérédité*, 1895.

Fifth, as a general rule, the higher an animal is in the zoological series the more complex is its ontogenesis. At the same time the progress towards complexity need neither be uniform nor constant. The highest of one group of animals may have an ontogenesis much more complex than the lowest of the group next in order above it. There is a specificness even in this matter, and there is no complete chain of types, representing a regular sequence of ascents.

Sixth, there is a general principle which may be stated in several different ways, and which has given rise to an immense amount of discussion. It has also been called the "great law of biogenesis." It may be enunciated in this way—that ontogenesis never follows a simple and direct route, but reaches its end by detours (" ces détours de l'évolution," *Delage*). In the forming of the completed embryo there are stages passed through which apparently serve no useful purpose; there are organs which appear and disappear again leaving sometimes rudiments which confessedly are dangers to the organism; some of these transitory organs have a temporary use, but others seem to have none at all. The higher vertebrate embryo, for instance, has three sets of urinary organs—the pronephros and its duct, the mesonephros and its duct, and the metanephros and its duct; and yet the necessity for some of them is not apparent. Further, it has for long been noted that many of these "detours" or temporary organs and parts distinctly recall the stages or appearances seen in animals lower down in the zoological scale; and so it came to be thought that in ontogenesis there is a sort of recapitulation of Comparative Anatomy, or, to put it in more modern terms, that ontogeny gives a condensed phylogeny, or that there is a reminiscent projection of phylogeny into ontogeny. Before, however, we discuss the correctness of this conclusion, let us see that we have a clear idea of what is intended by this general principle, this "great biogenetic law."

Henry Drummond[1] gave a picturesque and vivid description of what he understood and read into it. He wrote: "The human embryo is a subtle phantasmagoria, a living theatre in which a weird transformation scene is being enacted, and in which countless strange and uncouth characters take part. Some of these characters are well known to Science, some are strangers. As the embryo unfolds, one by one these animal actors come upon the stage, file past in phantom-like procession, throw off their drapery, and dissolve away into something else. Yet as they vanish, each leaves behind a vital portion of itself, some original and characteristic memorial, something itself has made or won, that perhaps it alone could make or win—a bone, a muscle, a ganglion, or a tooth—to be the inheritance of the race." So Drummond pictured the human embryo "wandering among the ghosts of departed types"; in making a man, "Nature introduced the framework of these earlier types, displaying each crude pattern by itself before incorporating it in the finished work." "Every creature that lives climbs up its own genealogical tree before it reaches its mature condition."

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[1] Drummond, H., *The Ascent of Man*, p. 87, 1894.

This law, which as we shall see is not so really a law as has been thought, may be stated in another way. Apparently the framework of the body is not laid down once for all, but is rather constructed in portions and even in overlapping portions, so to speak. One part of the framework may be replaced in whole or in part by a new substructure often of a type quite different from that which has preceded it. Readjustment, adaptation, alteration, and variation are processes constantly at work in the life of the embryo; it is by reorganisation that order is brought out of the seeming chaos of the results of blastodermic activity. If one were to imagine a builder constructing a palace by first erecting the scaffolding for a cottage; by then, after building operations had only just been commenced, replacing this by the scaffolding for a villa; and that again by the framework necessary for a mansion; and then, finally rearranging, and as far as possible utilising, all the materials for the formation of the palace; one would have an idea, albeit an imperfect one, of the character and complexity of ontogenesis. The comparison is, of course, almost ludicrously inadequate, for it gives no indication of the marvellous manner in which in organogenesis all the materials of the temporary scaffoldings are made use of in the construction of the permanent edifice, are worked into it so exactly as to be indistinguishable from each other in it. Only here and there in the body, in the appendix vermiformis, the fossa ovalis, and the ductus arteriosus, are to be seen the traces of some parts of the earlier formations which have either been incompletely utilised or have been imperfectly replaced by the later productions.

This same general principle of ontogenesis may be set forth in yet another way, as evolution by atrophy. In order that a new scaffolding may be set up it is necessary that the former atrophy; if a new plan of construction is to be followed it is needful that the old plan be abandoned. To quote from Ernest Mehnert[1] (as rendered by J. Arthur Thomson[2]), involution and evolution go hand in hand. The ovum develops, the polar bodies degenerate; the blastoderm develops, the merocytes degenerate; the head grows and the tail dwindles; the higher nerve centres of the mammalian brain increase and the occipital region diminishes; the metanephros comes and the pronephros goes; the backbone strengthens and the notochord disappears; and so on throughout a continual necrobiosis.

In whatever way it may be stated, there can be no doubt that in ontogenesis there is very evidently this principle of reaching the final result by ways which appear to be roundabout and by scaffoldings that are temporary. When, however, the attempt is made to find a constant and determining rule or law dominating the ontogenetic detours and the developmental scaffoldings, difficulties at once emerge; the explanation that the embryo of the higher vertebrates passes rapidly through a series of stages which represent the permanent forms of embryos lower in the zoological scale breaks down at once upon close examination, and as yet no other satisfactory hypothesis has arisen to take its place. But this fact demands a separate paragraph, and it will be best to embody it in a general principle, the *seventh.*

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[1] Mehnert, E., *Biomechanik erschlossen aus dem Principe der Organogenese*, Jena, 1898.

[2] Thomson, J. A., "Mehnert's Principles of Development," *Natural Science*, xiv. 385, 1899.

Seventh, then, it may be affirmed that ontogeny does not give a short recapitulation of evolutionary progress; it is not an epitomised phylogeny. This is seen in the fact that the time at which an organ appears in individual development does not always indicate the historical or phylogenetic age of that structure. If there is, then, a recapitulation in ontogenesis it is one in which Nature makes mistakes; or, to express the matter in more scientific language, there are "time-displacements" in development. For instance, the heart is regarded as a secondary differentiation (due to functional adaptation) of that part of the primary ventral blood vessel where the greatest resistance has to be overcome; but in the organogenesis of the human subject the heart appears before the associated main vessels. The mammary glands, also, make their appearance in the individual before the sebaceous glands from which they are supposed to have been differentiated; and the paired eyes in vertebrates arise long before the much older pineal eye. It would seem, to revert for a moment to a non-scientific way of speaking, as if Nature in telling in the individual the story of his descent (or ascent) made occasional slips and put incidents in a wrong order of occurrence. Doubtless the mistakes are only seeming mistakes, and an explanation is hidden away somewhere if it could but be found. Possibly, as Mehnert suggests, when an organ rises in physiological importance and structural differentiation it acquires a proportionate increase in its rate of development. Progressive organs are accelerated in their rate of development, and retrogressive ones tend to be belated; and their state of acceleration or belatedness (or retardation) is due to the intensity of developmental energy in them. It is not yet clear what exactly it is that exalts or depresses developmental energy. It must apparently be conceded, therefore, that ontogeny is not in point of the sequence of events a recapitulation of phylogeny; but it does not necessarily follow that there is no tendency for it to be so. It would seem that there is a constant inclination towards a chronological parallelism between ontogeny and phylogeny, along with frequently occurring interruptions and disturbances due to circumstances possibly of an environmental or hereditary character. It is not true then that "every creature climbs up its own genealogical tree," but it would seem to be true that it tries to do so; perhaps it sometimes swings from branch to branch! At the same time, even if the recapitulation principle be accepted in this partial form, it must not be forgotten into how marvellously short a story has been condensed so inconceivably long a history. In the first six weeks of the antenatal life of the human embryo are represented in epitome all the ages that have gone to the making of man! And each life adds on something to the ever-lengthening tale!

Further than these seven principles it does not seem wise in the present state of our knowledge to go. It would be easy, extremely easy, to add to the number, but the additions would be hypothetical generalisations, and they would also be hypotheses about which embryologists are far from being in agreement. There is, for instance, the question whether the various parts of the embryo exist already in the ovum and need only to be rearranged during organogenesis, whether each organ, each tissue, and each cell is represented by a distinct rudiment (*anisotropy* of the ovum); or whether the substance of the ovum is homogeneous and contains no parts specially set aside to form definite structures in the embryo, whether it is *isotropic*. The weight of evidence is apparently in favour of the isotropic character of the ovum; but it would seem as if in certain animals it were sometimes, and in others always, anisotropic. The evidence is chiefly of an experimental kind, and is not free from fallacy. At any rate, it is obvious that under the circumstances it would be unwise to attempt to formulate a general principle on the data at command. The same remark applies to the problem of the causes and manner of the differentiation of parts in the embryo, to that of morphogenesis, to that of regeneration, and to many other biological questions.

Enough has been said to show that there are general principles in Embryology, general laws, the appreciation of which will facilitate the understanding of the architectonic phase of antenatal life. The outstanding peculiarity of Embryology is still its complexity, for the statement of general principles does not lessen that—it rather throws it into bolder relief; but surely behind this complexity there is a real simplicity if we could find out the great determining factor in embryo-formation. The results of the action of gravity are complex enough, but behind their perplexing manifestations is the simple law of gravitation. There may be some such simple and universally applicable principle of ontogenesis, if it could only be discovered. We need for Embryology an Isaac Newton "of an extraordinary genius and proficiency in these things."

CHAPTER III

Chronology of Embryonic Life: Preliminary Considerations: Conditions found (1) at the Beginning of the Second Week after Impregnation; (2) at the End of the Second Week; (3) at the Beginning of the Third Week after Impregnation; and (4) at the End of the Third Week: Recapitulation.

In this chapter and in the three that follow it an attempt is made to give a chronological sketch of the phenomena of embryonic life. The period of antenatal existence from the appearance of the first rudiments of the embryo in the embryonic area up to the transformation of that embryo into the neofœtus is dealt with. The neofœtal period, as readers of the first section of this Manual (p. 80) will remember, is the transition time intervening between embryonic and fœtal life. Its leading character—gradual assumption by the embryo of a recognisably human appearance—has been already described (pp. 80–84), and need not be referred to again. Let the reader, however, try to carry in his mind the visual image of the chief changes of these two eventful weeks (the seventh and eighth) of antenatal life, when the facial region becomes clearly and unmistakably a face, when the limbs become truly limb-like and no longer bud-like, when the caudal projection ceases to project as a free appendage, and when a wonderful series of internal alterations, including the commencement of the ossification of many of the future bones, accompanies the external modifications. Let him also remember that the neofœtus is, from the point of view of its physiology, foreshadowing the fœtus in its increasing dependence upon its placental connections.

It is with the embryo, then, before the neofœtal epoch that we have to do in these four chapters. The terminus of embryonic life we fix at the end of the sixth week of intrauterine existence. But at what time may it be said that the typically embryonic life of the new organism begins? We have announced the *terminus ad quem*, but what declaration have we to make regarding the *terminus a quo*?

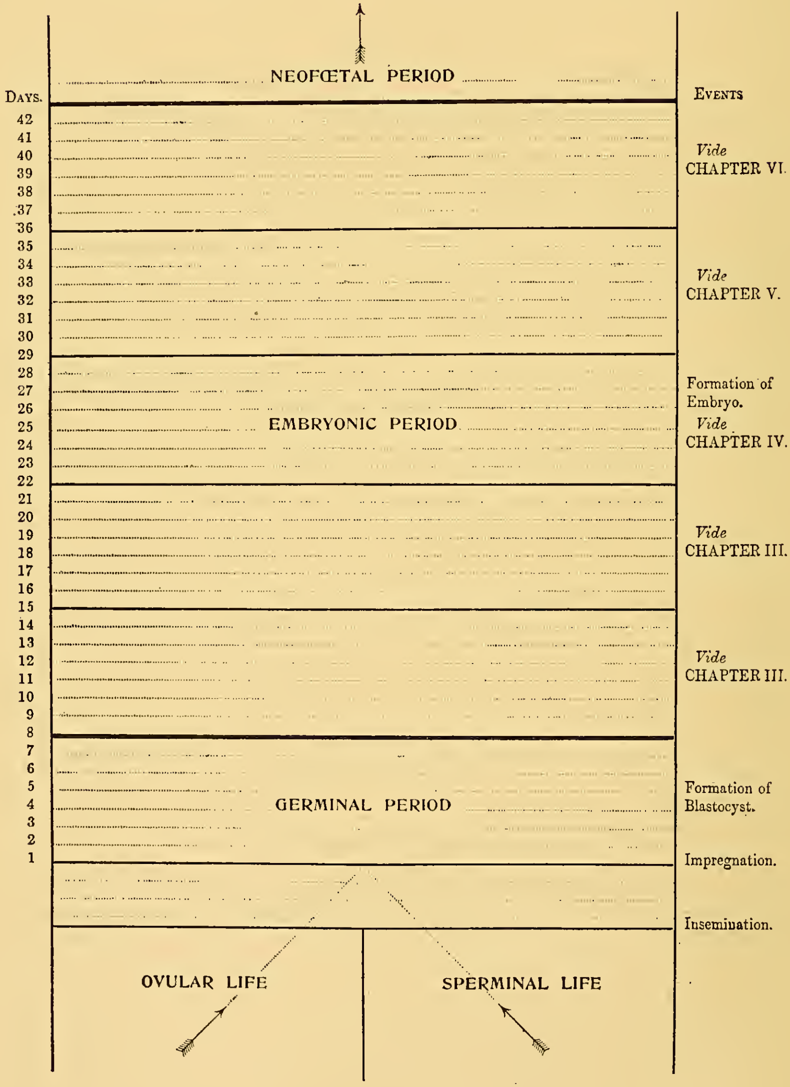
It may be admitted at once that it is not yet possible to fix exactly the date when human embryonic life begins and germinal existence ceases. If we regard the antenatal life of forty weeks as beginning with the impregnation of the ovum by the spermatozoon, then true embryonic life must manifestly begin at a date later than that. How much later, however, we are not in a position to state. If we allow a week, we are probably giving too much; if we decide upon less than a week, we may not be giving enough. In the absence of exact information, shall we say a week? Shall we let it be understood that provisionally we regard the beginning of truly embryonic life as coinciding with the beginning of the second week of antenatal life, reckoning from the date of impregnation of the ovum? I am reminded that we do not know at what time subsequent to coitus impregnation occurs. That I know well, and I have, therefore, in my scheme of the divisions of antenatal life (Fig. 1), set apart a period of half a week during which the delegated spermatozoon is presumably travelling towards the destined ovum. I make the supposition that three and a half days after coitus impregnation occurs and antenatal life in its unified form (*i.e.* within the walls of one cell) begins; a week later I presume that embryonic existence commences with the appearance of the first rudiments of the embryo in the embryonic area; and in five weeks after that I assume that typically embryonic life is over and neofœtal existence has begun. This conception is shown in schematic form in Fig. 2.

These exact periods of time are not, of course, insisted upon. They are advanced only as possibilities, which may turn out to be probabilities, but which may also prove to be quite otherwise. I do not indeed think it likely that it will be found that the whole period of antenatal life in the ordinary sense of the term (say, forty weeks or two hundred and eighty days) is an exact multiple of embryonic existence. Our knowledge of Nature's operations and mode of working out her results does not lead us to expect that she deals with exact multiples, as we understand them. Nature, we can well believe, in her calculations is not limited to the simpler exercises of arithmetic; she can deal with fractions!

Let us commence our study of the chronology of embryonic life by realising how important it is that we should form in our mind a visual image of the human embryo in the various weeks of its kaleidoscopic existence. It is a most difficult task; nevertheless, however difficult it is, it must be attempted, else all efforts to form rational ideas regarding the pathological phenomena of these embryonic times must end resultless or in error. In the later weeks (*e.g.* the fifth and sixth) of intrauterine life, the difficulties are not so overpowering, for observations of human embryos of these ages are not wanting, and conclusions may fairly be drawn from them. But in the early weeks! We know almost nothing of human blastoderms of less than seven days' age, we know but little of embryos of the second week, and even up to the end of the first month embryological facts are scanty. The *quæsita*, indeed, are many, but the *data* are few. So the embryologist has been driven to study the early stages in the lower animals, and has not always been careful to distinguish between the occurrences which are met with in them, and those which there is good evidence to show take place in the human embryo. In the text-books the details of Comparative Embryology are often interpolated among those of Human Embryology; and writers, in transcribing from original sources of information, are oftentimes careless about distinguishing between what has been found, for instance, in the embryo chick, rabbit, or pig, and what in the human subject. All this is very discouraging, and, in order to correct many misapprehensions, it would

FIG. 2.

THE DIVISIONS OF EARLY ANTENATAL LIFE.



be well worth some embryologist's time and trouble to edit a text-book in which all the facts known certainly regarding the *human* embryo were printed in red letters. I do not depreciate the value of Comparative Embryology, but I deny that its data can be unquestioningly transferred to fill up gaps in our knowledge of Human Embryology. Human Embryology so constructed is simply a series of scanty facts laced together by a series of assumptions.

The Blastocyst in the Second Week after Impregnation.

A. At the Beginning of the Week.

What mental picture can we form of the human blastocyst as it exists during the second week after impregnation? Two things, at least, we may rest well assured of: (1) the appearances of the blastocyst at the beginning and end of this week will be very different, and (2) the embryo will, in size and apparent importance, seem almost insignificant in comparison with its annexa and the decidual membranes. Development is very rapid in these early days, and a week is a long time in respect of the changes which are effected in it. At a later date than the second week, the truly embryonic part of the new organism is little more than an appendage of its own vesicles and membranes, and it may be concluded that this character is still more emphasised at the time with which we have here to do. Of these two things we feel sure within measure, but of what else?

Let us try to picture to ourselves what has taken place towards the close of the first week after impregnation. The impregnated ovum, now doubtless a blastodermic vesicle or blastocyst, has found its way into the uterine cavity. In so doing it has not dropped into an open space, as diagrams deceitfully suggest to the mind's eye, but has insinuated itself between uterine walls in complete contact, and possibly may have had some difficulty in thus making its way. It passes some distance from the uterine orifice of the Fallopian tube down which it has come, perhaps creeping on amœba-like by means of the plasmodial syncytium with which it is covered, perhaps waved onwards by ciliary action aided by a partial uterine contraction, perhaps lifted forward by a sort of congestive elevation of the mucous membrane upon which it is resting (who can say?); at length it reaches its destined anchorage. But what is it that constitutes a suitable mooring place, and by what means is the anchorage rendered tenable? Perhaps there is found an area of mucous membrane without its epithelial covering (or its cilia) where the blastodermic vesicle can reach connective tissue; perhaps there is a little slit in the mucosa under the margin of which it can edge itself and so get below the surface; perhaps it simply rolls into the furrow between two ridges and lies there till the swelling ridges meet over it and shut it in; perhaps it falls astride a ridge, and projecting downwards on each side of it fills also the adjacent furrows, and so remains till neighbouring parts grow up and around it; perhaps it bores its way downward through the epithelium by the destructive or phagocytic action of its covering cells, and the little opening through which it passes is closed with a coagulum. It is easy to multiply suppositions. Curiously enough one of the most obvious suggestions—that the ovum passes or sends processes into the mouths of the uterine glands—is that which nearly all embryologists nowadays agree in rejecting, and that apparently on good grounds.

According to the view we take of the manner of mooring of the ovum in utero will be the theory we hold of the mode of formation of the decidua reflexa (*s. capsularis*). John Hunter's conception of its origin has been abandoned, but there seems no reason sufficient to warrant the abandonment of the name which he gave to it; names in medicine do not always retain their original and etymological meaning. I shall, therefore, still use the term decidua reflexa, without, of course, holding the Hunterian view of its formation.

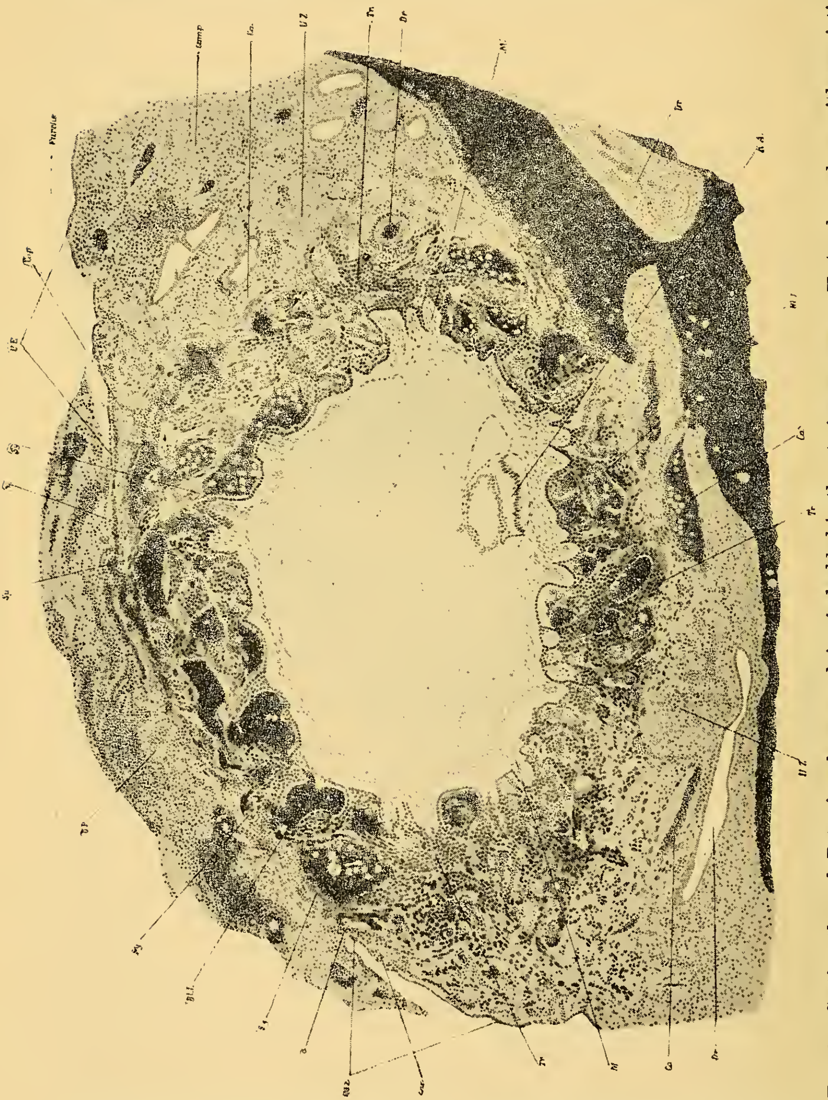


Fig. 3.—Section through Peters' early ovum, lying imbedded in the uterine mucosa. *K.A.*, the embryo with amniotic sac and umbilical vesicle; *U.E.*, uterine epithelium; *Cap.*, decidua reflexa (capsularis); *Tr.*, trophoblast; *Ca.*, maternal capillaries; *Dr.*, glands; *Bl.L.*, blood-pools; *Comp.*, compact layer of decidua; *M.*, mesoderm; *G.P.*, spongy tissue. (After Peters.)

H. Peters' specimen (*Ueber die Einbettung des menschlichen Eies*, Leipzig u. Wien, 1899) gives us the means of imagining how the reflexa is formed, for its age was five or six days, and this decidual membrane was still in process of differentiation. The specimen showed the ovum entirely sunk in the compact layer of the decidua vera about the middle of the posterior wall of the uterus. Over each side of the ovum was an extension of the vera forming the outermost portion of the reflexa, and the central portion was made up of a mass of fibrin. It may be supposed, therefore, that the ovum, after sinking down into the decidua vera, begins to excavate laterally as well as deeply; and so it comes about that the overhanging rim of the mucosa (the vera) forms the reflexa, while the opening made by the ovum is plugged with a coagulum of fibrin. In Leopold's earliest specimen (*Uterus und Kind*, Leipzig, 1897), the age of which may be stated as the end of the first week, the reflexa is seen surrounding the ovum entirely, but it is thin and fibrinous in its polar portion, and the outer surface of the ovum is intimately attached to it (Fig. 5). The differentiation of the mucosa forming the decidua vera into a compact (surface) and a spongy (deeper) layer is quite evident at this age; in the reflexa near its base are some glands lined with cubical epithelium, in the interglandular tissue are some large deeply-stained cells (maternal or fœtal?), and there is no epithelium on the inner aspect of this reflexa.

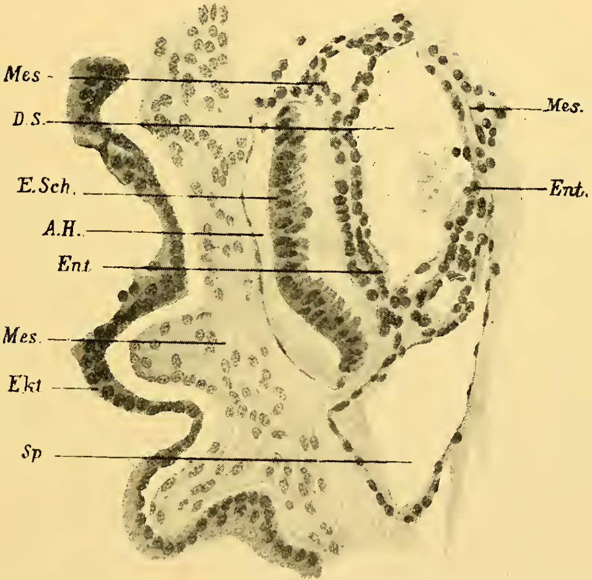


Fig. 4.—Section through embryonic part of Peters' early ovum. *A.H.*, amniotic sac; *D.S.*, umbilical vesicle; *E.Sch.*, embryo; *Ekt.*, ectoderm; *Mes.*, mesoderm; *Ent.*, entoderm; *Sp.*, fissure in exo-cœlom (?). (After Peters.)

The mucous membrane to which the ovum is moored or anchored is the serotina, now often called the decidua basalis or placental decidua. It consists, even at the age of Peters' specimen, of a superficial compact layer and a deeper spongy one. In the former part are signs of œdema with dilated capillaries and blood spaces, some of which communicate with lacunæ in the tissue surrounding the ovum (the trophoblast). In the spongy layer are small arteries. Large polymorphic cells are found in the compact portion, possibly decidual and maternal in nature, possibly also trophoblastic and fœtal. There is a loosening of epithelium going on in the glands of the serotina. In Leopold's specimen the serotina immediately below the ovum has half the thickness of the mucous membrane in its near neighbourhood; the surface capillaries open into the spaces (intervillous) between the processes of the trophoblast, so that even at this early date maternal blood bathes the outer aspect of the ovum.

In this manner, therefore, or in a manner somewhat like it (for it is unwise to draw deductions hastily from the interpretation of so few specimens), the fertilised human ovum becomes anchored to the uterine wall. The term *anchorage*, however, hardly meets the descriptive requirements of the case, when we think of the ovum surrounded as it is on all sides by maternal decidual tissues; it will be more correct to speak of it as planted in or imbedded in the uterine mucous membrane.

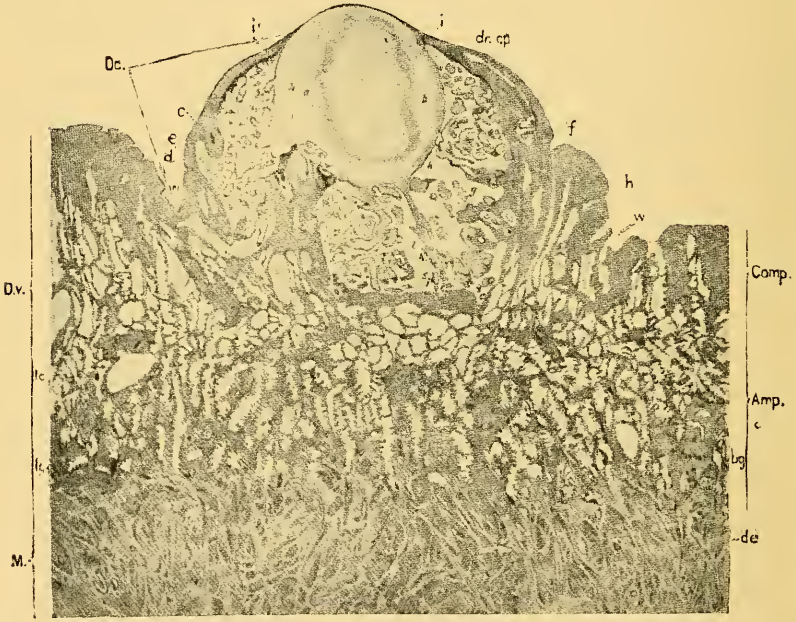


FIG. 5.—Section through Leopold's early ovum (end of first week of pregnancy). *M.*, muscular wall with ends of glands (*de*) in it; *D.v.*, decidua vera, with compact (*Comp.*) and spongy (*Amp.*) layers; *l.c.*, leucocytes in the lymphatics; *D.c.*, decidua capsularis or reflexa, in which up to *dr. cp.* gland spaces are seen, and above *i i* it consists mainly of fibrin; *b b* is the ovum or chorionic sac resting on a spur of the decidua; *a*, amnion; *d*, decidua serotina; *e*, mouth of maternal vessel; *h*, attached villi; *f*, imbedded villi. (*Vide*, Leopold's Atlas, *Uterus und Kind.*)

Let us now construct our mental picture of the ovum itself, as it lies thus imbedded at the end of the first week after impregnation. At this date it consists evidently of two very unequal parts, one of which may be called extra-embryonic and the other embryonic. Let us look first at the former part, which is not only much the larger of the two, but is also apparently of vastly greater importance. The ovular mass (blastodermic vesicle, blastocyst, chorionic vesicle, or whatever other name is given to it) has measurements varying from 1·6 : 0·8 : 0·9 mm. (Peters' specimen) to 4·0 : 3·7 mm. (Leopold's specimen); it is, therefore, a lenticular mass which lies thus in the uterine mucosa. Its outer aspect consists of a thick layer of what may be conveniently termed trophoblast, which has been probably developed from the epiblast of the ovum. In this trophoblast layer are numerous lacunæ and vacuoles, some of which, according to Peters, contain maternal blood. The processes or strands between the lacunæ consist of nucleated cells with distinct outlines, and near their outer ends some of them divide irregularly. In some parts the blood lacunæ are lined by a nucleated protoplasm in which no cell-outlines are visible, syncytial, therefore, in nature (Peters). Much difference of opinion exists as to the mode of formation of the syncytium which plays so important a part in the union between maternal and ovular tissues. Perhaps the most likely view is that it is formed by the action of the maternal blood upon the trophoblast cells; much of the protoplasm of the syncytium may then be of maternal origin, while its nuclei are the changed nuclei of the trophoblast (*vide* Bandler's article, *Amer. Journ. Obst.*, xlvi. 145, 1902). The trophoblast, it is thought, invades the compact layer of the uterine mucosa, while the maternal blood has a corrosive action upon the trophoblast cells, converting them into syncytium. It is to be noted that as yet there are no villi, but here and there processes of trophoblast make their way into blood sinuses in the decidua. We may provisionally call the interspaces intervillous. Beneath the trophoblast is a thin layer of mesoblast, but the latter scarcely passes at all into the processes formed by the former. In Leopold's early ovum there is a later stage of the development of the union between ovum and decidual membranes. In it the ovular mass is covered with villi (save in one small part); some of these are branched, some simple; some have a mesoblastic tissue core, others are purely buds of syncytium; some merely reach the decidua (serotina and reflexa), others are slightly imbedded in it; some show capillary formation in progress in them, others do not. Probably the villi in Leopold's ovum are the transformed strands of trophoblast seen in Peters' specimen. Between the villi are to be seen heaps of decidual cells, the beginnings, no doubt, of the trabeculæ which are found in later stages of development. In the intervillous spaces, also, maternal blood circulates freely, for maternal capillaries open into them.

It is to be noted then, that even at so early a period as the end of the first week after impregnation, the ovular mass is surrounded by a sort of primary placenta. The epiblastic proliferation or trophoblast would seem (as J. C. Webster states in his *Human Placentation*, p. 63, 1901) to have the following functions: it acts, first, as a means of attaching the ovum to the mucosa; second, its strands probably serve as pathfinders for the future permanent villi; third, it probably absorbs nourishment for the ovum from the decidual tissues and from the serum and blood with which it comes in contact. It is possible also that fragments of its syncytial covering may be broken off and travel into the maternal circulation (Bandler, *New York Med. Journ.*, lxxvii. 54, 1903), a possibility which takes on great importance when considered in connection with the development of deciduoma malignum and the pathology of pregnancy. The trophoblast, it may be added, may be regarded as the same structure to which the names of chorion, exochorion, primitive chorion + decidual layer, epiblast of non-embryonic part of blastodermic vesicle, and ectoplacental formation have been given by various writers. It is matter for great regret that there is such a plurality of names; it is probable that the term trophoblast will gradually supersede the others, with benefit to the reader who does not wish to solve troublesome terminological puzzles.

Let us now proceed with our inquiry regarding the constitution of the ovular mass at the end of the first week after impregnation. What lies inside the trophoblast? As has been said, there is inside it a thin layer of mesoblast (two to four thicknesses of cells, *Peters*), a little thicker opposite the pro-embryon. Its cells are rounded, oval, and spindle-shaped. Inside the sac formed in this way by trophoblast lined with mesoblast is situated at one point the pro-embryon (for we can scarcely yet call it "embryo"). Here between the mesoblast lining the trophoblast and the epiblast of the pro-embryon is placed a small cavity, that of the amnion. It is completely closed, and is lined with a layer of very flat cells opposite the pro-embryon and with the cylindrical cells of the embryonic region themselves. It is to be noted that in this earliest known specimen (*Peters'*) the amniotic sac is already closed, so that we can know nothing of its mode of formation; but the fact of its being closed suggests the question whether it was ever open. Probably the amnion in the human subject is not formed by the upheaval of folds of extra-embryonic somatopleure at all, but by a breaking down of epiblast tissue to form a cavity (Berry Hart), or by inversion of the blastoderm (Mall[1]). At any rate we have to put an amniotic cavity into our mental picture of the ovular mass at the end of the first week after impregnation. On the side of the amniotic sac next to the centre of the ovular mass is the epiblast of the pro-embryon, and to the inner side of it again is the umbilical vesicle lined with hypoblast cells and showing also some mesoblast cells outside these. In the pro-embryon or embryonic area, it is to be noted there is as yet no appearance of the primitive streak, so that an amniotic sac and an umbilical vesicle are in existence before any trace of the embryo itself appears. This, also, seems to be the state of affairs in F. P. Mall's early ovum (*Johns Hopkins Hosp. Bull.*, iv. 119, 1893). Neither is there any indication of a cord-like structure or Bauchstiel, for as yet the amniotic and umbilical sacs are, as it were, buried in the mesoblast of the chorionic vesicle. Graf Spee, who carefully examined Peters' specimen, could not be sure which was the cranial and which the caudal end of the pro-embryon. The remaining space inside the ovular mass is the extra-embryonic cœlom or simply the exo-cœlom.

Such then is the conception we have to form in our mind of the new organism in the uterus about the end of the first week after impregnation. It is, so to say, only a peep that we thus obtain of antenatal affairs at this early period. There is a great lacuna in our knowledge, a lacuna which extends from the time when the human ovum leaves the ruptured Graafian vesicle up to the time when it is found implanted in the uterine mucosa with its amniotic sac and umbilical vesicle closed and the decidua reflexa nearly completed. This gap in our knowledge we may attempt to fill up by observations upon the lower animals, but it is not safe to conclude that what occurs in them will occur in the human subject. We may also attempt to supply the missing parts of the kinematographic representation of the progress of formative processes from our imagination, but it is still less safe to pursue this plan. So we must be content to wait till yet earlier specimens of human ova are met with. It is the safest method, but the waiting may be long. Better, however, is it to wait for facts than to construct theories which have soon to be demolished.

B. At the End of the Week.

In order to picture to ourselves the state of affairs in utero towards the end of the second week after impregnation, we have the specimens of Graf

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[1] Mall, F. P., "Development of the Human Cœlom," *Journ. of Morphol.*, xii. 395, 1897.

Spee (12 days), Merttens (8 days (?) but probably more), F. Burgio (12 to 13 days), Reichert (12 to 13 days), Breus (12 to 14 days), F. P. Mall (13 days), Keibel (13 to 14 days?), Merttens (14 days), His (13 to 15 days), Leopold (14 to 15 days), Eternod, and some others.[1] Of course it must be remembered that these ages are only approximate, for it is extremely difficult from the history of the case to fix the probable age of the conception. Further, the appearances and measurements of the embryos cannot be used as definite guides, for there is some reason to believe that all embryos do not progress towards a given stage in their development with the same degree of rapidity. With these considerations in full view we may now proceed to form an idea of the condition of the new organism at the end of the second week.

At this date there exists, as all the specimens show, a distinct and recognisable Embryo; no longer have we to do with a pro-embryon or embryonic indication. At the same time, the embryonic part of the ovular mass is still insignificant in point of size when compared with the embryonic vesicles and the decidual membranes. We shall, therefore, first consider the decidual membranes, the chorion, the amnion, and the umbilical vesicle.

The decidua reflexa (capsularis) now forms a complete fold over the ovular mass, but the outer polar portion is mainly, if not entirely, fibrinous in nature, showing neither surface epithelium nor decidual cells, nor glands. The decidua serotina (basalis) exhibits clearly the division into a compact and a spongy layer. The outer parts of some of the glands are obliterated. Large decidual cells (many of them spindle-shaped) are seen in the compact layer, as are also many sinuses containing blood. Nucleated plasmodial masses are to be discovered lying among the decidual cells. In the spongy layer the gland spaces are large, and are lined with columnar or cubical epithelium. Decidual cells and plasmodium are also found in the spongy part. On the surface of the compact layer of the serotina next to the ovular mass is plasmodium or syncytium continuous with that covering the villi (for there are now distinct villi). The general opinion held at the present time is that this plasmodium is not formed from the original surface epithelium of the decidua or from that of the gland ducts, but in the way which has been already indicated (*vide* p. 23).

Inside the decidual membranes (reflexa and serotina) lies the ovular mass or chorionic vesicle (as we may now call it). It has a diameter varying from 3 to 5 mms., and it is furnished at this date with recognisable villi, no longer with simple strands of trophoblast. These villi are mostly simple, but a few are branched, and they may cover the whole chorionic vesicle or be defective at the poles; they measure about ·5 mm. in length; and they are attached to the decidua reflexa and serotina. They are covered with a coating of syncytium, and below that lies a layer of distinct cubical cells, Langhans' layer. Nearly all the villi have now a mesoblastic core of connective tissue. The syncytial covering of the villi is, as has been already stated, continuous with that on the surface of the serotina and reflexa. There are distinct intervillous spaces containing maternal blood, and into these spaces masses of syncytium here and there project. About this date (end of second week) capillaries are found in the mesoblastic core of the villi. At the point of attachment of a villus to the decidua there is usually a great proliferation of the cells of Langhans' layer, forming a distinct knob.

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[1] The references of the contributions in which these embryos are described will be found in Hertwig's *Handbuch der vergleichenden und experimentellen Entwickelungslehre der Wirbelthiere*, Jena, 1901–1903, and in other recent Text-books of Embryology, *e.g.*, that of M'Murrich.

What now are the contents of the chorionic vesicle at this age? Attached to the inner aspect of the chorionic vesicle by a stalk (Haftstiel, Bauchstiel, anlage of the umbilical cord) is a mass which consists of the amniotic sac, the umbilical vesicle, and the embryo (Figs. 6, 7, and 8). The amniotic sac is closed, and it covers the dorsal surface of the embryo lying close to it; on the ventral surface is a wide opening leading from the hypoblastic or entodermal interior into the umbilical vesicle. Both the amniotic sac and the umbilical vesicle are small structures in comparison with the chorionic vesicle. The embryo, measuring about 1·5 mm. in length, consists of a mass of cells lying between the amniotic sac and the umbilical vesicle, and continuous at its caudal end with the Haftstiel or umbilical stalk. In it can be recognised a primitive streak (thickening of epiblast cells), and in front of it a canal (the neurenteric) by which the amniotic sac communicates with the archenteron which is now showing signs of division into an intra-embryonic part (the gut tract), and an extra-embryonic part (the umbilical vesicle). In front of the opening of the neurenteric canal is the medullary plate with the two medullary folds forming the medullary groove which is not yet converted into a canal. These parts are formed by a thickening and an infolding of the epiblast; similarly on the ventral surface there is an infolding of hypoblast which gives rise to the notochord, which is at first a hollow rod of cells communicating at its posterior end with the neurenteric canal. In some of the specimens said to be of the age we are now considering, namely, end of second week after impregnation, there are indications of five or seven protovertebræ (the primitive segments of Minot, *Urwirbel* of the Germans) in the mesoblast near the notochord. There may also be a trace of the anlage of the heart near the cephalic end of the embryo in the form of two tubes in the mesoblast. According to Graf Spee there is, about this time, a small diverticulum from the single cavity of the gut tract and umbilical vesicle into the Bauchstiel, which he regards as the beginning of the allantoic duct (Fig. 8). Vessels also can be recognised in the wall of the umbilical vesicle; it is not clear that these yet communicate in any way with the heart rudiment to constitute a vitelline circulation. In Eternod's specimen (*Anat. Anz.*, xv. 181, 1898) there was a curious, hitherto undescribed vein in the caudal part of the umbilical vesicle ("anse veineuse vitelline"); there was also a single allantoic vein due to the fusion of the original two veins.

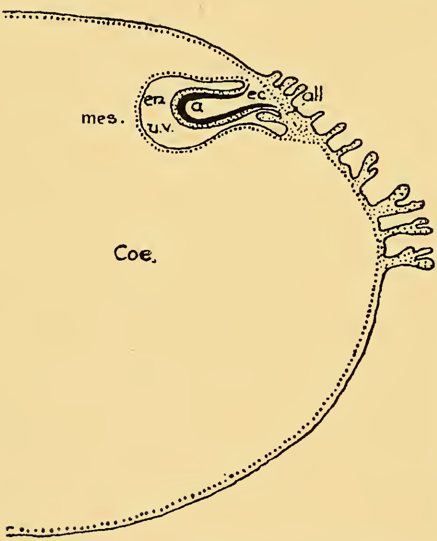
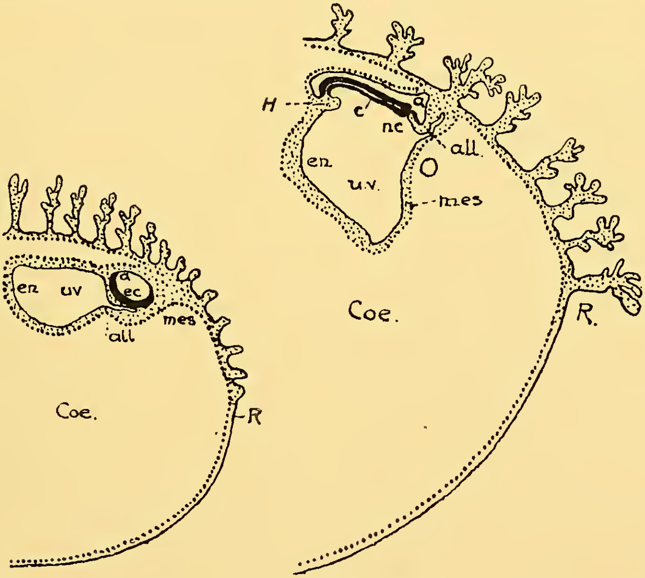


Fig. 6. — Diagrammatic section of one-half of Mall's early ovum. Enlarged 10 times. The villi are only shown in part. *Ec.*, ectoderm; *en.*, entoderm; *mes.*, mesoderm; *u.v.*, umbilical vesicle; *coe.*, cœlom; *all.*, allantois; *a.*, amnion. (After Mall.)

Such is, perhaps, as complete a picture as we can yet form of the appearance of the chorionic vesicle and its contents at this period of antenatal life. It leaves, of course, much to be desired. We know nothing of the changes taking place in the human ovum as it comes down the Fallopian tube. We know not how it develops its thick covering of epiblast cells or trophoblast. We can only suppose that soon after its arrival in the uterus it is furnished with a covering, apparently possessing all the cellular activity of an epithelioma, by means of which it eats its way into the mucosa of the uterus. While it has all the cellular activity of an epithelioma (and more), it, however, has not the unrestrained or ill-regulated mode of growth of such a tumour, for very soon an orderly development of parts begins to be evident, and a primitive placenta is evolved, while embryonic membranes, vesicles, and structures commence to appear. From the point of view of the antenatal pathologist it is much to be regretted that there is no specimen showing how, in the human subject, the amniotic sac is formed and how the umbilical vesicle arises, for these are structures which are supposed to have much to do with the origin of teratological conditions. In the earliest known human ovum both these structures are already present, and they give no indication as to their ontogenesis.



Figs. 7, 8.—Diagrammatic section of two early human ova. Enlarged 10 times. About half of each is represented, and the villi are outlined over only a part of the ovum. *R.*, Rauber's layer; *a.*, amniotic sac; *u.v.*, umbilical vesicle; *ec.*, ectoderm; *en.*, entoderm; *mes.*, mesoderm; *all.*, allantois; *c.*, notochord; *n.c.*, neurenteric canal; *H.*, position of heart. (After Graf Spee and Mall.)

The question of the age and size of human embryos is a very difficult one. F. P. Mall's settlement of it is the best that we have at the present time. Mall (*Johns Hopkins Hosp. Bull.*, xiv. 29, 1903) has found that for embryos of from one to one hundred millimetres in length their ages can be fairly correctly estimated by multiplying the length in millimetres by one hundred, and then extracting the square root, when the result will be the age in days. The formula is $\sqrt{100 \times \text{length in mm.}} = \text{age in days}$. For fœtuses of from 100 to 220 mm. in length, the length in millimetres equals the age in days. It is useful to remember the following leading facts, which are fairly well established: embryos of 1 mm. are about 12 days old; of 2·5 mm., about 14 days; of 4·5 mm., about 19 days; of 7 mm., about 26 days; of 11·5 mm., about 34 days; and of 17 mm., about 41 days. After forty-one days the embryo becomes the neofœtus, and its later measurements will be found in the first section of this Manual, which deals specially with the fœtal period of antenatal life.

The Embryo in the Third Week after Impregnation.

Several embryos of the third week are available to enable the embryologist to construct his picture of developmental events at this period; but, as it happens, there is a scarcity of material showing the state of the decidual membranes at this time. It is truly an *hebdomada mirabilis* for the embryo, this third week after impregnation, for during it there is a marvellous differentiation of organs and tissues taking place, and a transformation scene going on, the details of which are so complex as to baffle the keenest observer. We cannot trace out the processes in their intricacy, but we can at least recognise the results.

Through the growth of the chorionic vesicle and its contents, the decidua reflexa comes in contact with a larger surface of the decidua vera, and the potential space between these two membranes is diminished; for at the beginning of this third week the chorionic vesicle measures 14 mm. by 12 mm. by 5 mm. (Leopold's fifteen day specimen). Decidual cells are seen in the reflexa as well as in the serotina, and in the lower and middle part of the former there are enormously distended capillaries. In the compact layer of the serotina are likewise numerous dilated capillaries. The outer ends of the glands are very narrow, appearing as slits. In the spongy layer the gland spaces are irregular, and contain much desquamated epithelium. Here and there are extravasations of blood. The relations of the ovum to its membranes are well seen in Guicciardi's fifteen days' specimen (Fig. 9).

The mode of attachment of the chorionic vesicle to the reflexa and serotina is such as has been already indicated. Possibly the villi are even now becoming more numerous in relation to the serotina than to the reflexa, indicating the commencement of the differentiation of the chorion into a villus-carrying part (chorion frondosum, placental part) and a portion which is bare (chorion læve, non-placental part). As yet, however, there is a circulation going on all round the chorionic vesicle (in its reflexal as well as in its serotinal part), and no indication of a limitation of it to any one area. The villi are covered with syncytium with Langhans' layer underneath, and in their mesoblastic cores capillaries can be clearly seen. In Guicciardi's specimen (*Ann. di ostet.*, xxiv. 176, 1902) only a few villi were vascularised.

With regard to the structures inside the chorionic vesicle in the third week, it has to be noted that the amnion is at first a thin membrane springing from the body of the embryo round the origin of the umbilical vesicle. It, therefore, surrounds the back, sides, and cephalic and caudal ends of the embryo, but has no relation as yet to the umbilical vesicle (or yolk-sac) and to the part of the embryo which communicates with that vesicle. It is closely applied to the embryo, there being as yet little liquor amnii. During the third week the amniotic fluid increases relatively in amount, but even at the end of the week the membrane is not far removed from the embryo, and does not surround the umbilical vesicle and scarcely

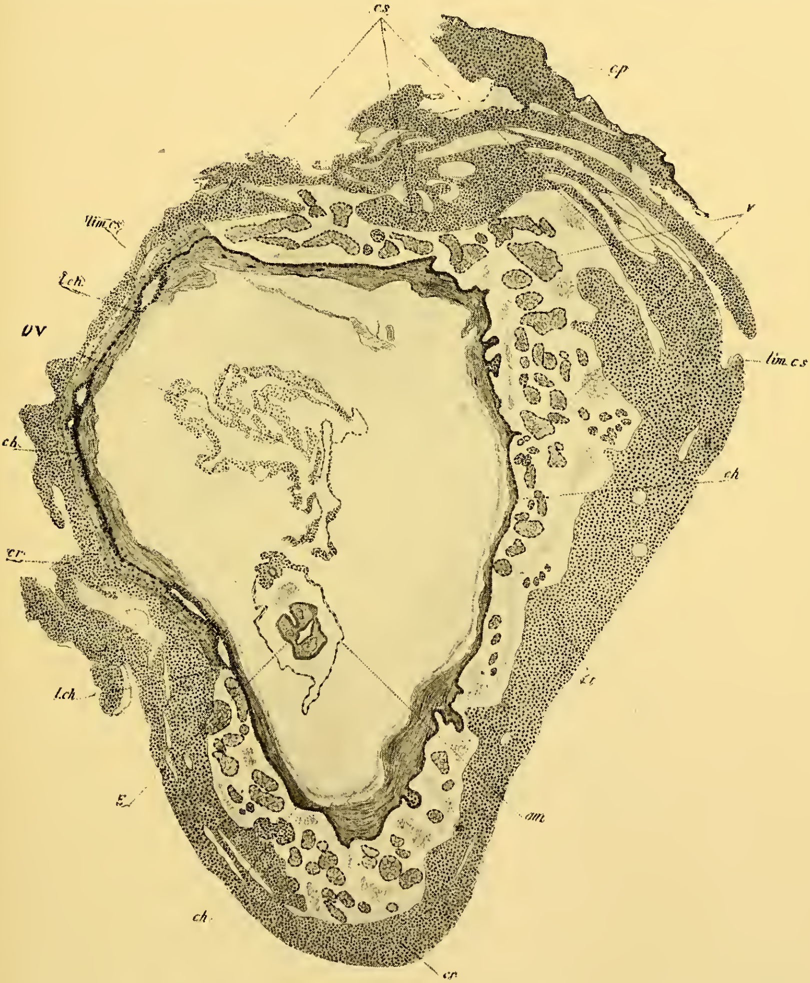


FIG. 9.—Guicciardi's Early Gestation Sac. Section showing—*cs.*, caduca or decidua serotina, at one pole of ovum; *cp.*, decidua vera; *cr.*, caduca or decidua reflexa; *v.*, chorionic villi; *lch.*, tract in which the chorion comes into relation with the decidua, a zone of amorphous tissue alone intervening; *ch.-ch.*, chorionic epithelium and connective tissue; *am.*, amnios; *E.*, embryo; *UV.*, umbilical vesicle. (*Vide Annali di ostetricia*, xxiv. p. 176, 1902.)

covers the heart. In its microscopic characters the amnion about this period shows a differentiation: there is an epiblastic layer of somewhat endothelial cells as before, but the mesoblastic tissue now consists of an outer layer similar in appearance to the epiblast, called the mesothelium, and of an inner homogeneous matrix next to the epiblast layer.

Embryo at the Beginning of the Third Week.

For our knowledge of the appearances of the human embryo, about the beginning of the third week after impregnation, we are indebted to the study of the specimens of J. Kollmann, of C. S. Minot (Nos. 195 and 143), of His (Lg, Sch. 1, and L), of A. Rondino, and of Coste. The embryo now measures from 2·2 mm. to 2·5 mm., and is still almost insignificant in size when compared with the chorionic vesicle and the decidual membranes; but it already shows a marvellous advance in the differentiation of its parts (Fig. 10). The cephalic and caudal ends are quite recognisable, and both of these project a little beyond the umbilical vesicle, which is now no longer attached to the whole length of the ventral aspect of the embryo. (In Kollmann's 2·2 mm. embryo the umbilical vesicle was attached for a distance of 1·5 mm., leaving the head to project 0·58 mm. and the tail 0·3 mm.) The cephalic end is already showing signs of enlargement, a feature which is so characteristic at later stages of embryogenesis, and is bending slightly towards the ventral aspect. There may be no branchial arches (Kollmann's embryo), or there may be two (Minot's Nos. 143, 195) or three (Coste's). No indication of the eye or ear may be found (Kollmann's embryo); or the optic vesicles may have already grown out, and the epiblastic invagination which is to form the otocyst or auditory vesicle may have begun to form (His' Embryo Lg). The oral invagination can be seen, but the oral plate still separates it from the large primitive pharynx; below

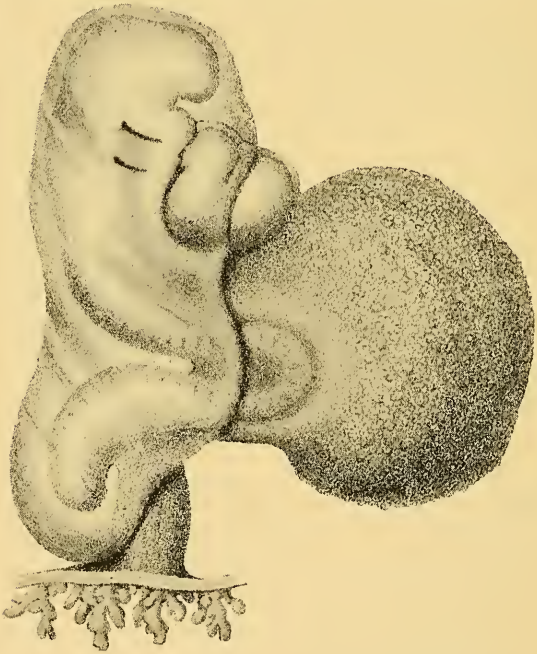


Fig. 10.—Embryo at the beginning of the third week.
Embryo Lg. (After His.)

it is the first branchial arch, which by and by becomes the mandible, and below that is the first branchial slit, or rather groove, with the second or hyoidean branchial arch. The brain (vesicular in character) forms a large part of the whole embryo: there is a fore-brain from which the optic vesicles have grown out; at the junction between the fore- and mid-brain there is a sharp bend forwards (almost at a right angle) of the former part; the hind-brain is relatively very long, and near its centre lies the open invagination of the otocyst (Fig. 11). The greater part of the medullary groove, therefore, is now closed in to form the medullary canal; the part posterior to the hind-brain is not yet differentiated into the spinal cord. Between the fore-brain and the attachment of the umbilical vesicle, and lying in a large pericardial space, is the prominent heart, which consists of an inner tube formed of endothelial elements, and an outer tube of contractile elements, which ultimately form the heart muscle. This heart tube is asymmetrically bent: from the point where the great veins enter it, it runs towards the head and left side, making the auricular limbs; then it

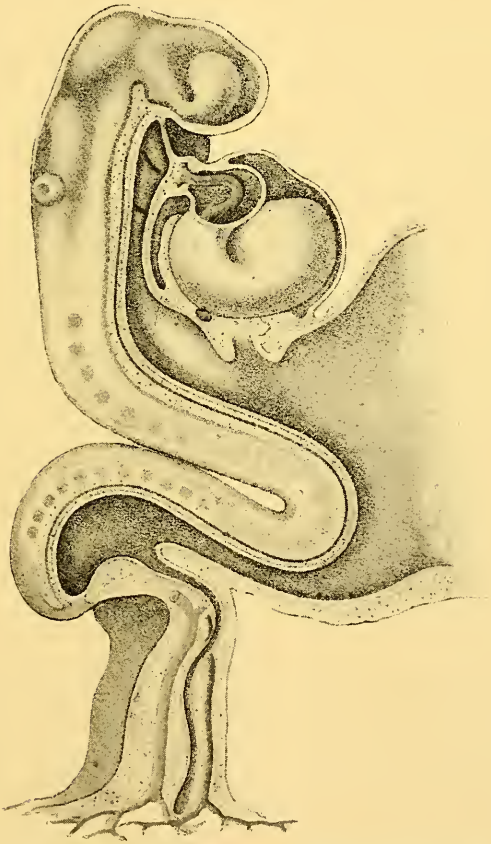


Fig. 11.—Embryo at the beginning of the third week, seen in section. Enlarged about 37 times. (After His.)

turns to the ventral side and obliquely to the right, forming the ventricular limb; and then takes a curving course to the median line, forming the aortic limb, and ends close behind the mouth. Between the two heart tubes (endocardial and myocardial) is a considerable space; and the inner or endothelial tube is continuous at one end with the walls of the veins and at the other with those of the aorta. We note, therefore, that by this date the two endothelial tubes, which represented the heart in the second week, have fused into or become one. From the aortic limb (outside the pericardial sac) arises the aorta, which divides into two branches on each side which, as the aortic arches, pass round the pharynx. The front branch on each side curves over and joins the second, to form one of the two dorsal aortæ. The dorsal aortæ pass towards the caudal end of the embryo; about midway they fuse into one dorsal aorta, which near the tail bifurcates into two vessels (the allantoic or umbilical arteries), which pass through the Bauchstiel (or allantoic stalk) to the chorion. In an earlier stage, doubtless, the dorsal aortæ pass, without fusing, to the umbilical vesicle as vitelline arteries, but of this we have insufficient evidence from human embryos. The veins which proceed to the heart consist of the cardinal, the jugular, the omphalo-mesenteric or vitelline, and the umbilical. On each side of the body the jugular vein (from the head end of the embryo) joins the cardinal vein (from the tail end) to form the ductus Cuvieri, which passes into the sinus venosus and through it into the heart. The ductus Cuvieri is joined by the umbilical or allantoic vein of the same side, which comes from the chorion by way of the Bauchstiel, and then takes, as Minot says, a short cut through the somatopleure along the base of the amnion. The omphalo-mesenteric or vitelline vein opens into the sinus venosus. There is as yet no trace of the inferior vena cava, and, since nothing more than a slight evagination or outgrowth from the fore-gut represents the liver, the veins have not the complicated hepatic relations which they afterwards develop.

With regard to the intestine or embryonic part of the archenteron at this age, it is to be noted that it is divided into three parts. Of these the fore-gut is expanded anteriorly into the wide primitive pharynx with two gill-pouches. The middle portion communicates freely with the umbilical vesicle, and shows the anlage of the liver just where it is continuous with the fore-gut. The posterior portion is distinct from the umbilical vesicle, and ends in a dilatation (His' bursa), and from the under surface of this dilatation arises the allantoic diverticulum which passes into the Bauchstiel (*vide* His' Embryo Lg, Figs. 10 and 11). As already stated, the fore-gut is shut off from the oral invagination by the oral plate (Rachenhaut).

At this period (beginning of third week after impregnation) the notochord can be seen distinctly, flanked with a varying number of protovertebræ, or, to use Minot's more correct term, primitive segments. These primitive segments, which perhaps even at this age show a division into the myotome next to the medullary canal and the nephrotome (or intermediate cell mass) which lies distally, vary in number from fifteen (Kollmann's specimen) to twenty-nine (His' Embryo Lg). One of the most remarkable features presented by embryos of the beginning of the third week is the presence of what has been called the dorsal flexure (seen well in Minot's Embryo, No. 195, and in His' Embryo Lg). By this term is meant the bending of the column of primitive segments in such a way as to form a deep dorsal concavity, possibly in order to accommodate the long back of the embryo. Minot says about this (*Human Embryology*, p. 313, 1892): "the facts indicate that the back is too long for the somatopleure at the side of the body, and that it finds room . . . by becoming concave; later it springs into a new position of equilibrium by becoming convex; it is possible that the change from the concave to the convex position is very abrupt, and it is probable that the time of its occurrence is very variable." This flexure may sometimes owe its existence to accident, but I agree with Minot that His' observations prove it to be normal in certain instances at least. From the teratologist's point of view, its presence is particularly interesting, as it is apparently maintained permanently in some monstrosities (*e.g.* in iniencephaly and exomphalos, *vide* Plates 15, 16, 17, and Fig. 28).

In order to complete our survey of the state of the embryo at this epoch, we must now glance at its caudal extremity. The prolongation of the body of the embryo by which it is attached to the chorion has now become a distinct stalk (Bauchstiel, body-stalk, allantoic stalk, later the umbilical cord). On account of the bending forwards of the caudal extremity of the embryo, the origin of the Bauchstiel likewise comes to be situated more on the ventral aspect. The stalk contains at this date the allantoic arteries and veins, and the allantoic diverticulum from the archenteron. It is appreciably nearer to the wide stalk of the umbilical vesicle, but it has not yet come into contact with it.

Embryo at the end of the Third Week.

We form our visual image of the human embryo at the end of the third week after impregnation from the study of the specimens of Chiarugi, His (Embryos, Rf, M, BB, and Lr), Allen Thomson, Ecker, Hecker, von Baer, J. Müller, and R. Wagner. Organogenesis is still proceeding at a very rapid rate, for the embryo at the end of the third week differs in many particulars from the embryo at the beginning thereof; and we have not nearly enough observations of human embryos of these ages to enable us to fill up the gaps in our knowledge of the means by which one stage passes on into the next. It is undoubtedly a wonderful week (*hebdomada mirabilis*) in the history of the embryo; all the story of embryological development is wonderful, but the third week is so essentially a week of beginnings that it arrests our attention, fascinates us, and finally amazes us by the variety and complexity and rapidity of the changes which supervene upon these beginnings. When the first rudiment of an organ or part has appeared, it is not so difficult or so surprising to follow it in its progress into its mature form; but to see it emerging in the first instance out of a sort of pre-embryonic chaos, that it is which startles, astounds, and almost stupefies us. Had not one of the writers of old time a dim adumbration of all this when he wrote these words?

> "Thine eyes did see mine unperfect substance,
> And in thy book were all my members written,
> Which day by day were fashioned,
> When as yet there was none of them."

To return to the description of the embryo at the end of the third week, it may be stated generally that all the systems and parts which were found indicated at the beginning of the week are now much further advanced in development, while some new parts have for the first time become evident. The umbilical vesicle is now attached by a relatively much smaller base to the ventral aspect of the body than formerly, so that we may reasonably begin to speak of the pedicle of the umbilical vesicle or yolk-stalk; the vesicle itself has become pear-shaped. It is still growing, indeed it continues to increase till the end of the fourth week, but its rate of growth is slackening. The embryo measures at this age from 2·66 mm. (His' Embryo M) to 3·2 mm. (His' Embryo BB), or even to 4·2 mm. (His' Embryo Lr). The measurements of the whole chorionic vesicle may be 7·5 mm. × 8·0 mm. (His' Embryo M), or 11 mm. × 14 mm. (His' Embryo BB), or 12 mm. × 9 mm. (Ecker's Specimen), or 12 mm. × 12 mm. × 9 mm. (Chiarugi's Specimen).

The head projects well beyond the umbilical vesicle, and shows a slight twist to left or to right; this twist is part of the spiral form which the whole embryonic body has assumed, the caudal end exhibiting a twist to the opposite side as compared with the head. There are now three (or four) branchial grooves. The mouth is relatively large; it is deeper than at the beginning of the week on account of the rupture of the oral plate; it communicates, therefore, with the fore-gut (Fig. 12). On each side of the mouth at its upper corner can be seen the maxillary process from the first branchial arch or mandibular process, which is also very evident. The pharynx is still wide, and four pouches can be easily recognised; each pouch lies between two branchial arches. A new development is the presence of a small projection on the ventral floor of the pharynx in the middle line; this is the *tuberculum impar* of His; and from it arises part of the tongue. With regard to the nervous system, it must be noted that the medullary or neural canal is now closed in its whole extent. The fore-brain, which has become quite distinct from the mid-brain, is divided into two parts, the secondary fore-brain (prosencephalon or telencephalon) and the inter-brain (thalamencephalon or diencephalon); or rather, as Minot believes, the anlages of the cerebral hemispheres arise from the anterior end and dorsal side of the fore-brain, which, on account of the head bend which is present, grows downward and forward. The optic vesicles are by this time clearly stalked, and the otocyst is a closed pear-shaped vesicle. With regard to the primary head bend or flexure, to which reference has been made, it is to be noted that now it is so marked that no longer is the fore-brain at right angles to the hind-brain (by a flexure situated in the mid-brain), but it has become so

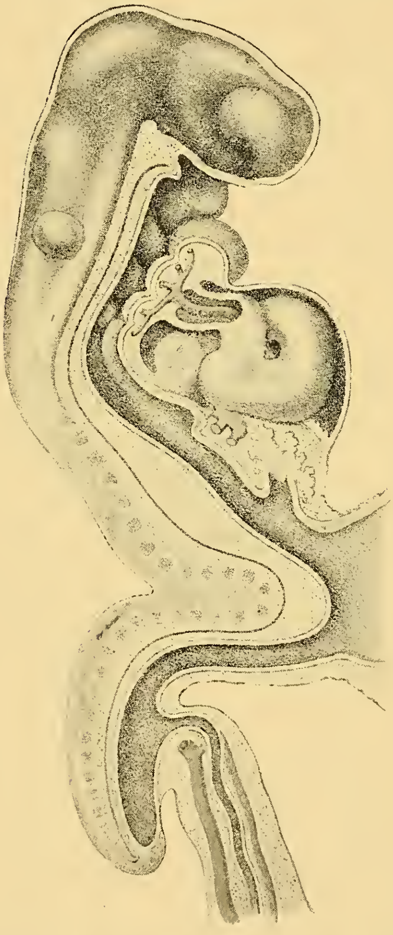


Fig. 12.—Embryo at the end of the third week. Embryo BB. Enlarged about 37 times. (After His.)

sharply bent that its floor is almost parallel with the floor of the hind-brain. It must be remembered that the fore-, mid-, and hind-brain are not at this stage of development anything more than vesicles. At the junction of the hind-brain with the spinal cord is the medulla oblongata, and in it even at this date it can be seen that the central canal is wider in the dorsal than in the ventral portion; at this point, also, there is an indication of the second cerebral flexure or neck-bend which appears first as a projection (His' *Nackenhöcker*). In front of this region is the anlage of the cerebellum, and behind it is the spinal cord.

The heart, as seen in His' Embryo BB, is now an S-shaped tube, "the venous end is convex toward the head, the arterial end convex toward the tail" (Minot). From the arterial end spring the aortæ which give off five branches (aortic arches) on each side of the neck; these branches unite again on the dorsal side, and passing backward the resulting trunk joins that of the opposite side to form the single median dorsal aorta, which subdivides into the two umbilical or allantoic arteries. Each of the aortic arches helps with the surrounding tissue to make a visceral or branchial arch; and between the five arches are the four visceral, branchial, or gill clefts or grooves (for they are never really clefts in the human embryo). The anlages of the true auricular cavities of the heart have now appeared, and the two limbs of the ventricle are nearer together and form a distinct apex where they join. The heart area of the embryo is quite covered by amnion at the stage of development at present under consideration. The veins consist of the cardinals and jugulars, of the ducti Cuvieri formed by their union, the omphalo-mesenterics and the umbilicals; the three last named come into close relation with the anlage of the liver and also with the septum transversum, while the cardinals are anatomically associated with the developing Wolffian bodies (to which I shall immediately refer). The development of the septum transversum and of the diaphragm is a peculiarly complex and obscure part of organogenesis; but upon it the researches of Franklin P. Mall (*Johns Hopkins Hosp. Bull.*, xii. 158, 1901) and others have thrown much light. The septum transversum is, to begin with, a V-shaped bridge of mesodermal tissue (irregular round cells, numerous vessels communicating with the veins of the heart) which connects the umbilical vesicle with the embryo at the juncture of the head with the amnion. It supports the omphalo-mesenteric and umbilical veins, and contains in it the anlage of the liver as well as that of the diaphragm, and all these structures are at a high level in the body of the embryo in the neighbourhood of the structures of the head; indeed nearly the whole cœlom at this stage of development lies in the head and neck region. The septum transversum serves to divide the cœlum anterior to it or headward of it (the parietal cavity of His) from that which lies posterior (tailward) to it (the trunk cavity of His); but laterally the two cavities communicate by passages, the parietal recesses, each of which divides later into a ventral and a dorsal part. Ultimately the parietal cavity becomes the pericardial sac, while the trunk cavity with the dorsal parietal recesses becomes the pleuro-peritoneal cavity. By the end of the third week the liver diverticulum, now enlarged and branching, is found embedded in the septum transversum. Through the descent of the septum all these associated parts greatly change their relations to the framework of the body.

At this date, also, traces of the Wolffian bodies can be recognised as little canals in the Wolffian ridges; the latter are longitudinal ridges, one on each side of the dorsal surface of the cœlom of the abdomen. The tubules of the Wolffian body (mesonephros) are evidently developed from the nephrotomes or intermediate cell masses of the primitive segments of the neighbourhood. The blood from these bodies passes to the cardinal veins. Thirty or more primitive segments or protovertebræ can be recognised (His' Embryos BB and Lr), and the dorsal flexure has now disappeared, a convexity taking the place of the concavity which was present at the beginning of the third week. A tendency is present for the embryo to bend forwards, the cephalic and caudal extremities approximating, and this tendency becomes more evident in the fourth week. The curving forward of the caudal end of the body brings the insertion of the Bauchstiel still more to the front, and so it and the umbilical vesicle lie nearer to each other than formerly.

Recapitulation.

Thus, in these two weeks, we see the embryo developing from a mere disc of tissue resting upon a relatively large umbilical vesicle into an organism with a circulatory apparatus, a series of vesicles constituting a nervous system, an intestinal canal, a body cavity with a commencing septum dividing it into a thoracic and an abdominal portion, a mouth consisting of a five-sided fossa, a pharynx with branchial arches and clefts, a series of mesodermic somites or primitive segments, and rudiments of eyes, ears, and Wolffian bodies. This organism no longer rests, insignificant in size, upon its umbilical vesicle, but is of relatively considerable size, and has its umbilical vesicle appended to it by a recognisable vitelline stalk. All these structures have appeared during these eventful weeks; and they have come into being by a series of changes of which we know very little from the direct examination of human embryos, but about which embryologists have formed many theories from the observation of the early stages of development in the lower animals. We cannot, in consequence, be at all sure of the manner in which many of the transformations and alterations have been produced. We know nothing, for instance, of the way in which the neurenteric canal is closed, and but little of the relation of the allantoic stalk to the Bauchstiel. In whichever direction we attempt to follow out the problems of the subject, we immediately feel the pressure of the limitations of our knowledge. At the same time the feeling of restriction thus produced must not be suffered to engender in us the idea that we are disqualified from ultimately searching out the secrets of organogenesis. When we think of the progress that has been made in the last twenty years, when we reflect how much the finding of such a specimen as Peters' early ovum may mean for the elucidation of our problems, and when we remember the hundreds of skilled workers engaged in this field of research, we take courage again and press forward. Every advance, it is true, but adds to our perception of the regions yet unknown; but this was to be expected, for the domain of Embryology is of vast extent. We are not, therefore, to be hindered but stimulated by the prospect ever opening up before us; the wider view is in itself a gain. Let us then go on carefully preserving early embryos, cutting them in serial sections, and reconstructing them again, so as to obtain an intimate knowledge of their inmost constitution. Scarcely any two will be found perfectly alike, and we may at any time make a discovery rivalling that of the detection of the neurenteric canal in the human embryo. Let us also examine all uteri and appendages removed by hysterectomy, vaginal or abdominal; such operations are common now-a-days; we may thus add to the number of the known specimens of early ova in situ in the uterus, we may even find an impregnated ovum in the tube on its way thither.

CHAPTER IV

Chronology of Embryonic Life (*continued*): Conditions found in the Fourth Week after Impregnation.

In the previous chapter an attempt was made to place in graphic fashion before the reader's mind a picture of the conditions found inside the uterus during the second and third weeks after impregnation. The picture was confessedly an imperfect one: many details were dimly represented because imperfectly known; others were only, so to say, outlined in the rough; while others were altogether wanting. Yet, after all, some idea was gained of the nature of the processes of organogenesis going on at this period of antenatal life. Let us now, in this chapter, try to do at least as much for the fourth week of embryonic existence. The attempt is likely to be more successful, for the number of known and examined specimens of embryos of this period is much larger than at the earlier dates. Let us pursue the same plan and consider first the extra-embryonic parts of the gestation sac and then the embryo itself.

Extra-embryonic Parts in the Fourth Week.

Regarding the decidual membranes at this period of intrauterine life we gain some information from the description given by E. Fraenkel (*Arch. f. Gynæk.*, xlvii. 139, 1894) of an aborted ovum, three and a half weeks old, and containing an embryo which measured 4·3 mm. in length and possessed thirty pairs of primitive segments. The sac formed by the decidua reflexa (*capsularis s. circumflexa*) measured 16 mm. in width at its base by 10 mm. in height. Two parts of the reflexa could be easily distinguished: a thin polar portion with no regular structure, with scarcely any traces of glands, and with signs of commencing degeneration; and a thicker basal portion, the inner half of which was more compact (no blood sinuses and very few glands), while the outer half, especially near its junction with the decidua vera, showed several gland orifices and many blood sinuses. The decidual cells were more compressed in the inner than in the outer half. In the decidua serotina the large decidual cells were practically limited to the compact layer. Blood sinuses could be recognised opening into intervillous spaces both in connection with the serotina and the reflexa. C. Kupffer's specimen, of about the same age, showed similar conditions (*München. med. Wchnschr.*, xxxv. 515, 1888); in this case also villi were found over the whole surface of the chorion although they were most strongly developed in an equatorial band. An epithelial double layer covered the chorion and the chorionic villi (Fraenkel's specimen), the outer layer being, as at an earlier date, plasmodial or syncytial, and the inner cellular. In the neighbourhood of the polar portion of the decidua reflexa the syncytium was very thick and was covered with a blood coagulum; in this spot the cellular layer was very thin. The stroma of the chorion reached its greatest thickness opposite to the decidua serotina. The villi were most numerous where the decidua serotina passed into the decidua reflexa. Kastschenko (*Arch. f. Anat. u. Entwcklngsgesch.*, p. 451, 1885) has described a fine network of threads in the syncytial layer at this age of pregnancy, and he found the syncytium thickest over the ends of the villi, while buds and strands extended from their sides in the form of processes. The amniotic membrane in the fourth week has very similar appearances to those described already (in the preceding chapter) as existing at the third week. The amniotic sac, on account of the rapid growth of the embryo, is at this time almost entirely filled by it, so that the amnion is closely applied to the embryo. This space between the amniotic sac and the wall of the chorionic sac, the extra-embryonic cœlom, is still large.

The umbilical vesicle or yolk-sac is now quite extra-embryonic in position, and is attached to the body by a more constricted pedicle, at first short and later of a considerable length. Towards the end of this week the Bauchstiel or allantois-stalk has grown partly round the proximal part of the yolk-stalk, so that we can now speak of the umbilical cord, although it is not yet very cord-like. The umbilical vesicle, in this week, reaches its greatest development; it measures from 2·7 by 3·0 mm. (His' embryo *a*) to 5·0 by 7·0 mm. (Mall's embryo of 26 days). The umbilical vesicle can be recognised as differentiated from the yolk-stalk, and the cavity in the latter (vitelline duct) is soon obliterated.

The Embryo in the Fourth Week.

For the study of human embryos of the fourth week (22 to 28 days) several specimens are available, among which may be named His' embryos *a*, D_2, W, R, B, A, Eck 1, and Stt, and those of C. Rabl, Coste, Allen Thomson (fourth embryo), Hensen, Ecker, Fol, B. H. Buxton, Mall, J. Müller, V. Magnus, and Waldeyer.

The embryo of this age measures from 5 to 7·5 mm. in length; but the organism is now so coiled upon itself that it is difficult to ascertain its real length. The dorsal flexure of the preceding week has entirely disappeared and is replaced by a well-marked and rounded convexity posteriorly, which is due to the approximation on their ventral aspect of the caudal and cephalic ends. The embryo is shaped like a C, the upper end of the C being the fore-brain and the lower end the embryonic tail; or, rather, the organism is so rolled up that its dorsal outline describes more than a complete circle (Fig. 13). In addition to the head-bend (in the region of the mid-brain), there is also a well-marked cervical flexure or neck-bend (at the posterior limit of the hind-brain); and the well-developed tail is sharply bent forwards at the sacral bend. So it comes about that the length of the embryo from the head-end to the tail-end does not represent the total extent of the organism, thus His' embryo *a* measured 4 mm. but when unrolled 13·7 mm.

The body shows still the spiral twist which was noted at the end of the third week: the head is bent to the right and the tail to the left in His' embryo *a*. The Bauchstiel or allantoic stalk is now becoming more stalk-like; on account of the marked ventral concavity of the trunk and the development of the tail, it lies near to the yolk-stalk and partly surrounds it, as has been already pointed out.

A very noticeable change in the external appearance of the embryo is now visible, namely, the indication of the limb-buds. Possibly they may be recognised in some specimens of the end of the third week; at any rate, they are quite distinct at the beginning of the fourth. They are at present no more than slight swellings or flat processes arising from the ridge (Wolffian ridge) which runs along the dorsal border of the embryonic somatopleure. In structure they consist of rounded mesoblastic cells with an external layer of epiblast. Each limb-bud has an upper, dorsal, or extensor surface, and a lower, ventral, or flexor one; and there are two borders, an anterior or cephalic, and a posterior or caudal. Into these limb-buds grow processes from the myotomes of a number (not less than seven) of the primitive segments. The extremities are at this time truly appendicular *buds* and not *limbs*, for they are quite unsegmented. The anterior ones are larger than the posterior. As I have pointed out in the first section of this MANUAL, the limbs belong to the outlying parts of the developing organism and so are late in showing differentiation; thus it comes about that in the fourth week, when other systems are far advanced in development, the extremities are only little mesoblastic outgrowths.

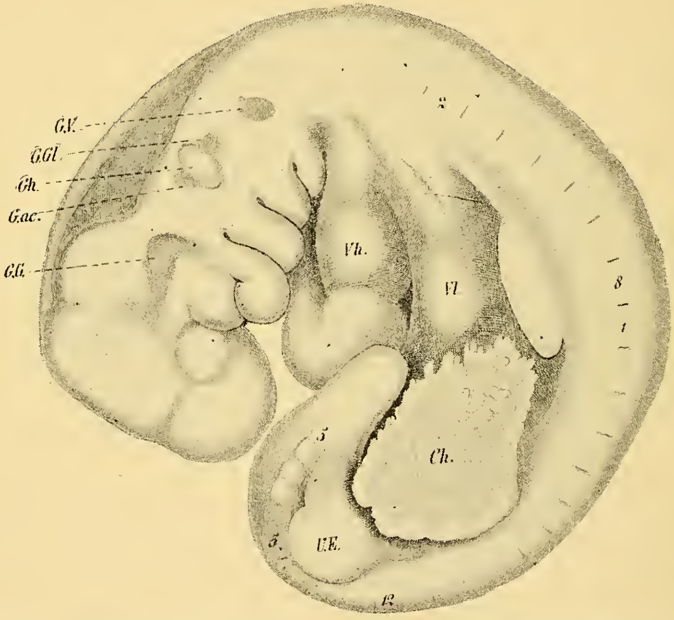


FIG. 13.—Embryo of the fourth week. Embryo *α* (after His). Enlarged 20 times. *G.V.*, vagus ganglion; *G.Gl.*, ganglion of glosso-pharyngeal; *Gh.*, otic vesicle; *G.ac.*, auditory ganglion; *G.G.*, Gasserian ganglion; *Vh.*, heart; *Vl.*, liver; *U.E.*, lower extremity; *Ch.*, chorion.

The embryo is still somewhat translucent, so that the internal parts can be dimly discerned. Thus it can be seen that there are at least twenty-seven primitive segments or somites (Mall's 26 day embryo, Figs. 14, 15, 16), and there may be thirty or more (cervical 8, dorsal 12, lumbar 5, sacral 5). There were thirty-five in Magnus' specimen. In the region of the head the outlines of the five chief divisions of the brain can be recognised, and the margins of the fossa rhomboidalis (future fourth ventricle) are distinct; the ganglia of some of the cranial nerves are also visible, and to them reference will be made below.

Three or four branchial grooves and arches can be made out during this week; they have irregular outlines, and are beginning to be transformed into the more permanent arrangement of parts. Towards the end of the week the sinus præcervicalis is well marked, and the fourth branchial arch lies deeply in it, and largely under cover of the third arch; the third arch, also, is within the sinus. This cervical sinus is formed by the growth of the second arch over the third and fourth arches till its tissues come into contact with the body wall beyond them in the region of the faintly marked fifth arch; thus the epiblast of these arches and clefts is buried. This change, however, is only beginning in the fourth week. From the dorsal or attached end of the first branchial or mandibular arch a projection can be seen arising; this is the superior maxillary process, and it can be recognised both in the beginning and towards the end of the fourth week (*e.g.* in His' embryo *a*, and in Mall's 26 day embryo). The ventral or free end of the first arch is knob-like, so also is that of the second or hyoid arch; in fishes it forms the operculum for the gills, while in the human embryo, as above stated, it serves to close in the sinus præcervicalis. It is to be noted that neither now nor at any other time do the branchial furrows or grooves in the human subject become continuous with the pharyngeal pouches; the epiblast comes into touch with the hypoblast (no mesoblast intervening) to form the "closing membrane," but there is no communication between the external branchial clefts and the internal pharyngeal pouches.

During this week another change in the external appearance of the facial region of the embryo occurs, the appearance of the first indications of a nose. On each side of the naso-frontal process which grows down between the two superior maxillary processes is an epiblastic thickening, the olfactory plate (as in His' embryo *a*); these two olfactory plates, after the twenty-fifth day, become hollowed out (or, rather, their margins grow up) to form the nasal pits (as in His' embryo *a* or in Mall's 26 day embryo). The pits, however, remain shallow during this week; further, their margins do not grow up on the side next the mouth, and so they open freely into the oral cavity. From the nasal pits the nasal mucous membrane ultimately develops. Just outside and anterior to the nasal pits are situated the optic vesicles which are now stalked and converted into optic cups; and each shows (at the end of this fourth week) a lens surrounded by a groove which also passes down between the superior maxillary process and the nasal pit of the same side. The lens is formed by the thickening of the epiblast at the point where the optic vesicle comes nearest to the surface. The otocyst or otic vesicle (formed from the auditory pit in the third week) has now receded from the surface of the epiblast or ectoderm; it becomes pear-shaped rather than spherical, and forms a labyrinth in which vestibular and cochlear portions and a recessus vestibuli can be dimly recognised.

Such are the more striking and evident external features of the embryo of the fourth week. We must now try to form a picture in our mind of the internal arrangements found at this epoch, and it will be convenient to study in order the nervous, alimentary, circulatory, urinary, and supporting systems of the embryonic body.

The spinal cord is the less differentiated part of the nervous system at this age, so it will be convenient to study it first. It consists of a tube with a central cavity which is still relatively large and has an elongated oval form, the long diameter of the oval being antero-posterior. The lateral walls are thick; the anterior and posterior are thin, and are called the roof- and floor-plates or mid-dorsal and mid-ventral laminæ. At the beginning of the fourth week two kinds of tissue-elements can be made out in the neural tube wall: spongioblasts or sustentacular elements and neuroblasts or young nerve cells (the future neurons). To begin with, the wall consists of a single layer of columnar cells or spongioblasts, but soon at the point where these cells border the lumen of the canal other elements appear between them called germinating or germinal cells, and from these arise the neuroblasts. The spongioblasts multiply and form the sustentative or sustenta-

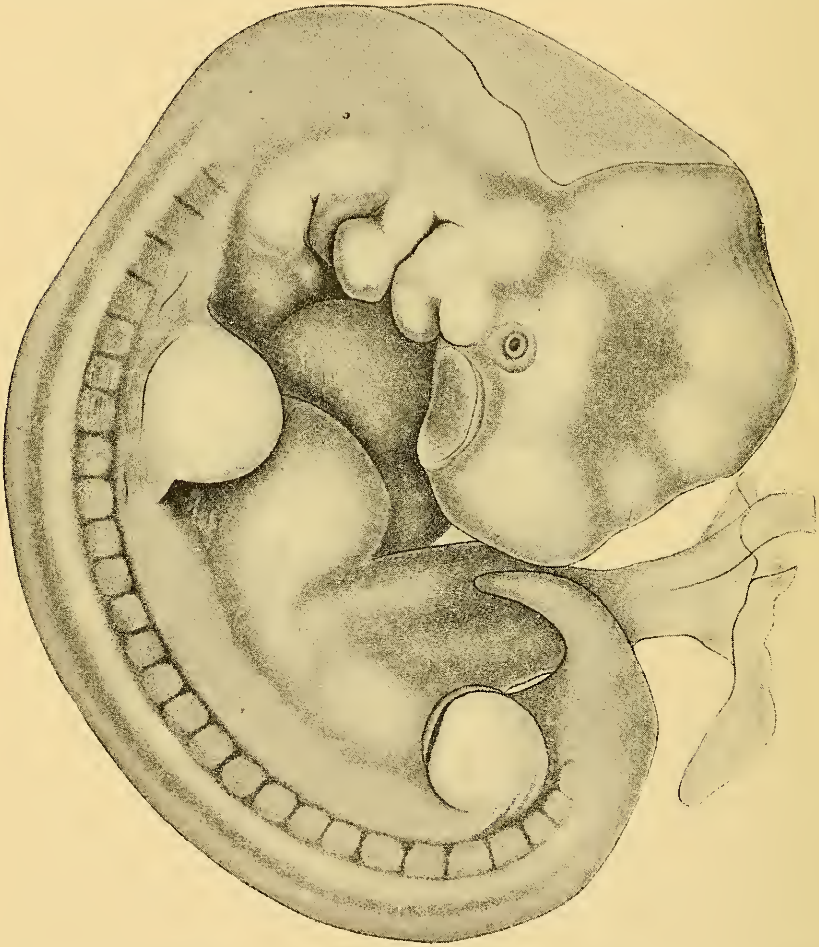


Fig. 14.—External appearances of Mall's 26 day embryo. Enlarged about 18 times. (*Vide* Mall's article in the *Journal of Morphology*, vol. v., 1891.)

cular part of the spinal cord, and more particularly what is called the neuroglia. The inner ends of the spongioblasts unite to form a close network next the canal cavity, the inner limiting membrane or ependymal layer. There is an outer layer formed by the branched prolongations of the ependyma cells, which forms the marginal velum or Randschleier of His. Between these two layers is a very delicate network, which becomes the mantle layer, and into its meshes the neuroblasts wander. This wandering would seem to take place by an accumulation of the protoplasm on the distal side of the nucleus, and this indicates the commencement of the formation of the axis-cylinder process or axon of the future neuron. Later, other processes arise from the neuroblast, the dendrites. The axons pass out through the marginal velum, and some form the ventral nerve roots.

While these changes have been going on inside the spinal cord the cells of the neural ridge or crest (line of union of the neural tube) begin to form the posterior or dorsal root ganglia; these cells arrange themselves segmentally at the sides of the cord, some of them (neuroblasts) take on a fusiform shape with a process extending from each end of the spindle, and one of these processes (the axon) grows inward, penetrating the marginal velum, to come into contact with the dendrites of the neuroblasts of the mantle layer. Thus the two nerve roots of the spinal nerves are developed, the ventral ones by cell processes growing outward, the dorsal ones by processes growing inward. Thus, also, a beginning is made with the differentiation of the cord into a grey and a white part, but as yet there is no contrast in colour, for the medullary sheaths of the nerves do not appear till the fifth month of antenatal life.

So far has the development of the cord progressed by the end of the fourth week that twenty-nine spinal nerves (cervical 8, dorsal 12, lumbar 5, and sacral 4) can be counted (Mall's 26 day embryo), each with a large dorsal ganglion and a ventral root. The ganglia are largest in the cervical region, and the eight cervical nerves are united by anastomoses, the future cervical and brachial plexuses. Posterior to the fourth sacral nerve, the dorsal ganglia are not fully separated from the spinal cord.

During this (fourth) week there are as yet no sympathetic ganglia to be recognised; but, from the first six dorsal nerves, branches extend towards the chorda dorsalis; and three of these lie in front of the cœliac axis and three behind it. From these branches arise the solar plexus and the splanchnic; at any rate this view commends itself to embryologists, for it brings the sympathetic into line with the cerebro-spinal system as derivatives of the epiblast or ectoderm. During development the cœliac axis comes to lie nearer the caudal extremity, and so the sympathetic twigs which surround it also lengthen.

The brain during the fourth week shows a marked increase in complexity, and requires careful study. Five parts of the neural canal in the cephalic end of the embryo can now be recognised: there is first the end-brain, telencephalon, or hemisphere-brain; behind it (above it topographically) is the inter-brain, 'tween-brain, diencephalon or thalamencephalon; behind it is the mid-brain or mesencephalon; and then follows the hind-brain or rhombencephalon, consisting of the two parts, the secondary hind-brain or metencephalon, and the after-brain or myelencephalon. Each of these parts contains a cavity. At the beginning of the fourth week the cavity of the telencephalon is single and communicates by a wide opening with the diencephalon; but towards the end of the week the hemisphere-brain is formed by two oval projections whose cavities are the future lateral ventricles, and they communicate with the rest of the cavity of the telencephalon, which, together with that of the diencephalon, forms the third ventricle. The openings between the lateral ventricles and the third are at this time very wide; later they become the foramina of Monro. There is a thin strip of tissue between the foramina of Monro, which is really the anterior end of the neural tube; it is called the lamina terminalis. The cavity of the hind-brain or rhombencephalon is represented in after development by the fourth ventricle; and the cavity of the mesencephalon, although now capacious, becomes the narrow iter, or aqueduct of Sylvius, of later dates.

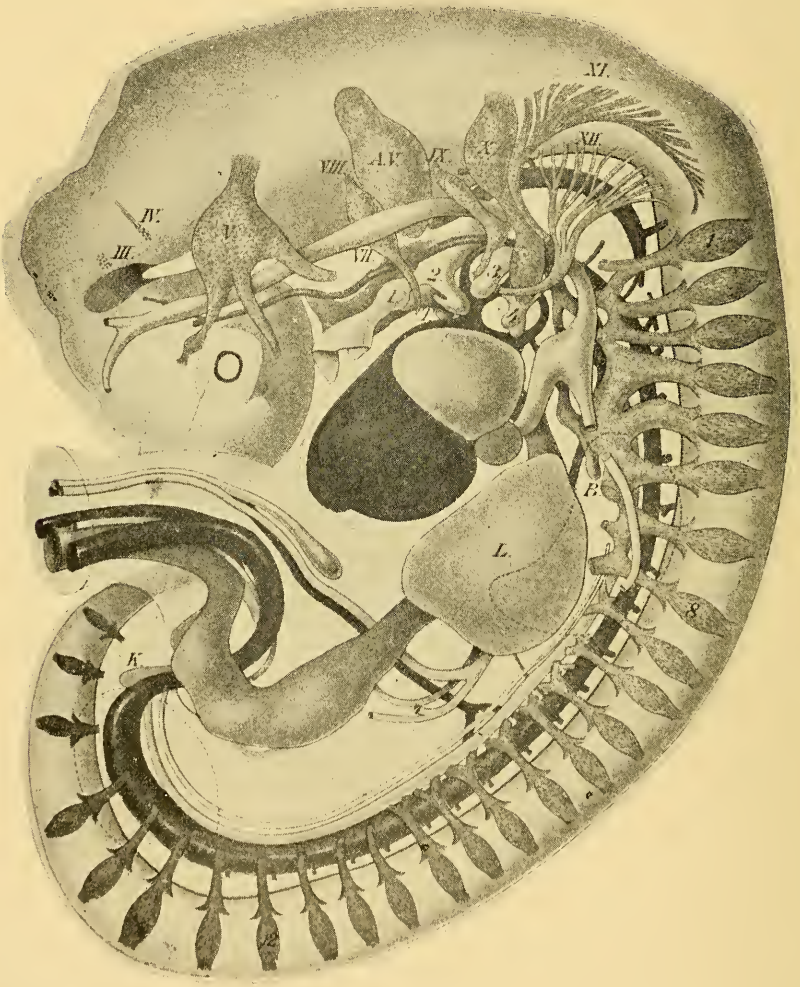


Fig. 15.—Reconstruction of Mall's 26 day embryo. Enlarged about 18 times. *III.* *IV.*, *V.*, etc., cranial nerves; *A.V.*, auditory vesicle; 1, 2, 3, and 4, branchial pockets; *T.*, thyroid gland; *B.*, bronchus; *L.*, liver; *K.*, kidney. The dotted lines mark the extremities; the spinal nerves and the blood vessels are indicated. (*Vide* Mall's article in the *Journal of Morphology*, vol. v., 1891.)

The mesencephalon becomes continuous with the metencephalon in a constricted portion, named the isthmus rhombencephali. Three flexures can now be seen in this region: the cephalic flexure in the neighbourhood of the mesencephalon, already noted and described in the preceding chapter; the cervical or nuchal bend, of which only an indication existed at the third week; and the pontine flexure in the region of the metencephalon, which is a flexure simply of the ventral side of the neural tube, and does not involve the whole head as the other two bends do. In the fourth week the cephalic and cervical bends are very marked, but the pontine one is only beginning to be indicated.

The walls of the neural tube in the region of the brain vary in thickness. Those of the mesencephalon and rhombencephalon are thicker than the parts anterior to them. In the myelencephalon the ventral wall alone thickens, the dorsal remaining very thin. The walls have the same general arrangement as in the region of the spinal cord: there is a roof-plate and a floor-plate, and between them are the thicker lateral walls which soon show the indications of a subdivision into a dorsal part or alar lamina, and a ventral part or basal lamina. These fundamental divisions of the neural tube are, before long, lost sight of in the great complexity of parts produced in the region of the brain; but they are there, although hidden, and have much to do with the architecture of this all-important part of the body.

The ganglia of some of the cranial nerves can now be recognised. At the beginning of the fourth week traces of the ganglia of the trigeminal or fifth nerve, of the auditory-facial, of the glosso-pharyngeal or ninth, and of the vagus or pneumogastric can be identified, although not very clearly; but by the end of the week their positions and relations, along with those of other of the cranial nerve ganglia, can be definitely ascertained. To take the nerves in their order, it has to be noted that the cells on the concave (oral) side of the nasal pit are pyramidal in shape, and have their bases directed towards the outside of the body; they may be regarded as an indication of the beginning of the olfactory or first nerve. There is as yet no trace of an optic nerve; the primary optic vesicle is still in communication with the cavity of the fore-brain, and in the secondary optic vesicle (optic cup) two layers of cells can be recognised—a proximal or pigment layer, and a distal or rods-and-cones layer (with a hyaline and a cellular zone). Even at this date a vessel, the arteria centralis retinæ, can be seen (Mall's 26 day embryo); it perforates the hyaline zone of the layer of future rods and cones. A possible indication of the origin of the third or oculomotor cranial nerve is found in the floor (basal lamina) of the mesencephalon; while there is a well-marked group of cells in the ventral wall (basal lamina) of the isthmus rhombencephali, from which the fourth or trochlear nerve arises.

The Gasserian (or semilunar) ganglion of the fifth or trigeminal nerve is quite recognisable, as is also a small group of cells upon its ophthalmic branch which constitutes the ciliary ganglion. Fibres forming the large sensory root (dorsal) pass from the ganglion into the hind-brain; the motor root arises more ventrally from the basal lamina of the hind-brain, and passes into the inferior maxillary division of the nerve. A group of cells in the basal lamina of the upper part of the hind-brain represents the sixth or abducent nerve. It is difficult at this age to separate the ganglia of the auditory (eighth) and facial (seventh) nerves; both these nerves arise from the alar lamina of the hind-brain. The acoustic ganglion is adherent to the auditory vesicle, which is pear-shaped, and has a prolongation from its dorsal side, which indicates the beginning of the aqueductus vestibuli.

Between the auditory vesicle and the myelencephalon or after-brain lies the upper ganglion of the glosso-pharyngeal or ninth nerve, which arises from cells in the alar lamina; on the ventral side is a second ganglion, the ganglion petrosum. The vagus nerve is represented by two large ganglia, the future ganglion nodosum and ganglion jugulare; these are united by a band of cells, and from the ganglion nodosum a branch passes to the fourth branchial arch. The spinal accessory arises in a row of bundles which lies

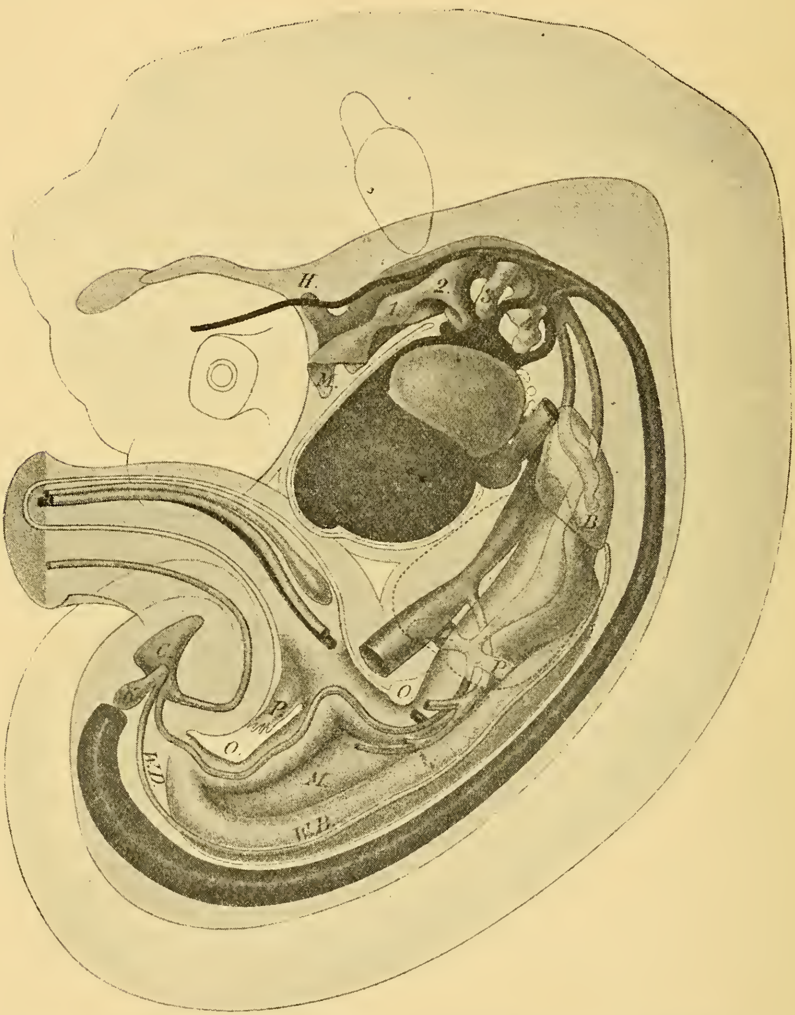


Fig. 16.—Deeper view of reconstruction of Mall's 26 day embryo. Enlarged about 18 times. *H.*, hypophysis; *M.*, mouth, mesentery; 1, 2, 3, and 4, branchial pockets; *B.*, bronchus; *P.*, pancreas; *L.*, liver; *W.B.*, Wolffian body; *W. D.*, Wolffian duct; *K.*, kidney; *C.*, cloaca; *O.*, openings by which the pleuro-peritoneal cavities communicate; *P.*, papilliform projection into the lower opening. (*Vide* Mall's article in *Journal of Morphology*, vol. v., 1891.)

between the vagus and the first cervical nerve, and emerges from the myelencephalon midway between its dorsal and ventral walls. In Mall's 26 day embryo (upon which this description is largely based) there was no trace of the rudimentary ganglion of the accessory, which has been found by His in the human subject; this is perhaps to be explained by the fact that it is an organ in process of degeneration, and so may be expected to be occasionally absent. The hypoglossal or twelfth nerve arises from a group of fibres parallel to but more ventral than those of the spinal accessory. It is evident, therefore, that already at the fourth week very considerable progress has been made with the ontogenesis of the complicated part of the mechanism of the nervous system known as the cranial nerves. It may be noted in passing that the trigeminus may be regarded as the nerve of the first or mandibular branchial arch and groove; the facial as that of the second or hyoid arch and of the groove in front of it; the glosso-pharyngeal as that of the third or thyro-hyoid arch and groove in front of it; and the superior and inferior laryngeal branches of the vagus as the nerves of the fourth and fifth branchial arches respectively.

Like the nervous system, the alimentary tract has likewise been increasing in complexity during the third week. The mouth cavity is still not clearly delimited from the pharynx. The *tuberculum impar* which becomes the buccal part of the tongue was noted in the third week; it arises from the first or mandibular branchial arch, and from the first interbranchial space; it now increases in size, and is marked off by the two alveolo-lingual grooves; and behind it is a V-shaped groove with a deep depression at its apex, the future foramen cæcum. The pharyngeal or posterior part of the tongue is formed from a thickening of the ventral ends of the second branchial arches, and into the angle between them the buccal part, so to say, fits. Behind the *anlage*[1] of the tongue is an inverted U-shaped ridge, the furcula, derived probably from the ventral parts of the third or fourth branchial arches, which later becomes the epiglottis. Behind it, at the end of the fourth week, is the narrow opening into the pulmonary diverticulum from the ventral aspect of the pharynx; from this diverticulum two lung buds have been evaginated, and these push their way into the isthmus of the cœlom (the neck of communication between the pericardial and peritoneal sacs), and form the pleural parts of the cœlom. The median part of the diverticulum forms the larynx and trachea. Rathke's pouch, an invagination found in the roof of the oro-pharyngeal cavity, has not yet come into contact with the infundibular prolongation of the telencephalon to form the hypophysis; this occurs in the fifth week. In the depression (foramen cæcum) behind the tuberculum impar, a bilobed body develops, which later constitutes the median lobe of the thyroid gland, and takes up a position lower in the neck. Thickenings of the tissues in the posterior and anterior walls of the fourth and third branchial furrows develop later into the lateral thyroids and the parathyroids; they are scarcely recognisable even as thickenings at this age.

The œsophagus is comparatively short on account of the high level of the diaphragm (septum transversum) at this age. The intestinal tube below the œsophagus is dilated slightly in spindle fashion to form the *anlage* of the stomach. In connection with the duodenum the *anlage* of the liver has now taken the form of two lobes, a right and a left; and it is said that the hepatic cylinders (future bile-ducts) possess a lumen. Another bud from the duodenum is recognisable at the end of this week: it is the small group of cells constituting the *anlage* of the pancreas, and it lies in the mesogastrium (the future great omentum). Below this level the intestine makes a loop toward the ventral aspect, and to this the yolk-stalk or vitelline duct is attached. The part of the loop above the vitelline duct, along with a portion of the part below, becomes the small intestine; the rest of the tube forms the large intestine, which at this age is chiefly constituted by the entodermal cloaca. The cloaca has a pyramidal form, the apex pointing tailward; there is, through the presence of the cloacal membrane, no opening of the cloaca on the surface of the body. The small tube known as the allantois forms a projection from the entodermal cloaca; and on each side of it and dorsally is the opening of a Wolffian duct. It is to be noted that the entodermal cloaca does not form the extreme caudal part of the intestine; that is constituted by the end-gut, which begins to wither during the fourth week. For the end-gut Berry Hart has proposed the name pars ultima, and for the entodermal cloaca that of pars penultima (*Trans. Edinb. Obst. Soc.*, xxvi. 259, 1901), and the nomenclature is concise and descriptive. About the end of the fourth week, or a little later, the penultimate part (entodermal cloaca) shows signs of division into an anterior and a posterior cavity by a coronal septum; the anterior cavity forms the bladder (according to the view of Keibel and others, strongly supported by Berry Hart, *Brit. Med. Journ.*, ii. for 1902, p. 773), the allantois only playing a subordinate part in its formation. The rest of the anterior cavity constitutes the urino-genital sinus, and the posterior part develops into the rectum.

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[1] Anlage, meaning the first outline or indication of a part or organ, is a useful German word with no exact English equivalent.

The consideration of the urinary organs at this date of embryonic life may be suitably taken up here in connection with the description of the entodermal cloaca, for, as has been stated, the Wolffian ducts open into this part of the primitive intestine. The Wolffian duct extends throughout the Wolffian body or mesonephros, on the dorsal side of it in the lumbar region, and on the ventral in the cervical. The Wolffian bodies are large lobulated structures, situated one on each side of the intestine from the cloaca to the sixth cervical nerve; glomeruli can be recognised in them from the sixth cervical to the fifth lumbar nerve, and there are about three glomeruli to a segment (in Mall's 26 day embryo). Just before the Wolffian duct enters the cloaca, a small blind tube arises from it; in process of time this is converted into the ureter and kidney (metanephros). This blind tube appears during the fourth week; it is not present at the beginning of it (*e.g.* in His' embryo *a*).

The circulatory apparatus, like the other systems of organs, shows marked developmental advances during this week (the fourth) of intra-uterine life. The separation of the single atrium into two auricles by means of a ridge growing from its dorsal and cephalic walls begins at this date; the separation, however, is incomplete, the opening between the auricles constituting the foramen ovale, or rather the ostium primum. The right auricle is larger than the left, and into it (the former) opens the sinus venosus or sinus reuniens, into which in turn open the vitelline and umbilical (allantoic) veins and the ducts of Cuvier. The opening of the sinus reuniens is guarded by a valve. The common atrio-ventricular canal is now divided by an incomplete septum into two auriculo-ventricular openings, by means of which the right and left auricular cavities communicate with the right and left ventricular cavities respectively, for by this time the common ventricular chamber is partly divided into two cavities. The two ventricular cavities, however, still freely communicate with each other, for the ridge or septum on the inside which corresponds to the sulcus interventricularis on the outside does not yet completely divide the ventricular space. The truncus or bulbus arteriosus is by the end of the fourth week nearly completely divided into two tubes. Already the symmetrical arrangement of the five aortic arches has broken down and been replaced by a new order. The third, fourth, and fifth arches of both sides persist, and these unite to form the two aortæ, which in their turn unite, between the sixth and seventh cervical nerves (in Mall's 26 day embryo), to form the single aorta. The aorta is much larger in the dorsal and lumbar regions than in the cervical, and in the lumbar region it divides abruptly into the two umbilical (allantoic) arteries. The pulmonary artery on each side can be seen arising from the fifth aortic arch as a comparatively small branch. The first and second aortic arches have by the end of this week (the fourth) apparently disappeared. The internal carotid artery with some branches can be recognised arising from the third arch. On each side of the dorsal aorta are (in Mall's 26 day embryo) twenty-one segmental arteries, the first being in front of the first cervical nerve, and the last behind the twelfth dorsal. The second segmental artery communicates with the vertebral, a large branch which extends forward to the region of the otic vesicle and gives off two twigs, the future anterior and posterior cerebellar arteries. The subclavians grow out from the dorsal aortæ, or from the segmentals opposite the fourth arches. Between the lateral and ventral sides of the aorta there are fourteen pairs of segmental branches which supply the Wolffian bodies. From the ventral side of the aorta the cœliac axis and the omphalo-mesenteric artery arise. Through the growth tailwards of the parts in the neck, including the heart and diaphragm, the origins of all these vessels are constantly moving backwards, as it were, in relation to the segments of the body.

The same general arrangement of the veins persists, with the exception that the left or sometimes the right omphalo-mesenteric or vitelline vein has now disappeared; the remaining vein (as portal vein) unites with the umbilical vein in the region of the liver, but before this happens it receives an inferior mesenteric branch. The liver is developed around the umbilical and omphalo-mesenteric veins. The cardinal vein (which receives the blood from the Wolffian body) joins with the jugular of the same side to form the ductus Cuvieri which opens into the sinus reuniens. Veins from the upper limb-bud (subclavian) also open into the duct of Cuvier or into the jugular vein. The jugular and cardinal veins also receive segmental branches. The right umbilical vein has usually disappeared by this time.

With regard to the supporting tissues of the embryo in the fourth week certain facts are well established. The notochord is still recognisable, and stretches from the caudal extremity to a point below the hind-brain. On each side of it are the mesoblastic segments (consisting of myotomes, sclerotomes, and cutis plates or dermatomes), and in its anterior part the vertebral arteries are also situated laterally. It is usually stated that cartilage does not begin to form in the sclerotomes till the second month, but Mall describes it already in his 26 day embryo. These sclerotomes grow round the notochord, and are transformed at a later date into the spinal column, the basi-occiput, and part of the basi-sphenoid. From the myotomes are formed the muscles of the body and limbs.

Like the weeks that precede it, the fourth is full of organogenetic activities. Construction is rapidly going on; it is true we have not to chronicle developments so astonishing as those of the third week, that *hebdomada mirabilis* to which reference has lately been made, yet those we have to deal with are wonderful enough, and in all respects more than difficult enough to explain or attempt to explain. We see the embryo beginning to assert itself even in the matter of bulk, while the umbilical vesicle has already reached its maximum size, and has more than reached its maximum importance. The curious dorsal flexure of the embryo has suddenly disappeared, and our visual image of the new organism now is a C instead of an inverted S; this C shape the embryo never quite loses again, and in the fœtus we recognise it in the familiar attitude of flexion; in a sense, there is even a reminiscent and instinctive assumption of it by the adult when in fear of bodily injury or hurt.

In this fourth week, also, there are seen for the first time the indications of limbs. They are nothing more than buds, it is true; but their advent is very striking, for we now realise what it was that gave to the limbless embryo part at least of its grotesque and non-human appearance. The embryo is still far from human in its aspect, the presence of the branchial arches and grooves quite prevents that. Not yet have these gill-like structures begun to disappear, buried from sight, in the cervical sinus; that fate awaits them in the next week. The first trace of a nose is now visible in the very unnose-like nasal pits, too shallow almost to deserve the name of pits; stalked vesicles represent the eyes; and the otocysts, by their retreat from the surface, have for the time removed even the suggestion of ears.

It is difficult to recognise the simple neural tube of the early days of development in the complicated series of brain vesicles of the fourth week; and yet the nervous system is only beginning to assume its labyrinthine form with its sinuous or tortuous passages, with the intricate ramifications of its cavities, and with its endless irregularities of contour, its invaginations and evaginations. We can still identify the central cavity of its various parts, for it is throughout fairly wide and canal-like, but soon this character disappears, and it is difficult to see in the narrow iter of later weeks the wide tract of the mesencephalon of the fourth week. Already the lateral walls are thickening irregularly, while the roof and floor in most parts remain thin and membrane-like. Quite at its anterior extremity this series of vesicles has begun to expand into that *magnum opus* of ontogenesis and organogenesis, the cerebral hemispheres: there is as yet little to be seen of that crowning superstructure of developmental activity; but its foundations are there, firmly laid, and even beginning to show above the surface. In the spinal cord, also, histological and structural differentiation is going on: spongioblasts are forming that neuroglia-network, in the meshes of which neuroblasts, potential neurons with potential axons and dendrites, begin to appear; and, having appeared, begin to stretch forth in bewildering fashion, and with far-reaching results so far as the later structure of this part of the nervous system is concerned.

Hardly less remarkable are the developments going forth in the great body cavity of the embryo, where we find an intestine with an

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end-gut or *pars ultima* and an entodermal cloaca (*pars penultima*), the *anlage* of a liver and pancreas, the indication of a trachea and lungs, and relatively large and well-formed Wolffian bodies. The last-named organs have, indeed, already reached their acme of structural differentiation and the culminating point of their developmental activity. The heart, also, is rapidly approaching the high degree of constructive detail which it maintains during the remainder of antenatal life; for, unlike the Wolffian bodies, it does not then start upon a degenerative progress, but remains permanently efficient and physiologically of great importance. Very soon its chambers, right and left, will be divided off from each other by septa, complete but for the presence of the foramen ovale, which serves as a communication between the auricles until the occurrence of birth and the replacement of the fœtal with the adult type of circulation.

CHAPTER V

Chronology of Embryonic Life (*continued*): Conditions found in the Fifth Week after Impregnation.

Extra-embryonic Parts in the Fifth Week.

In the fifth week after impregnation, the decidual membranes bear much the same relations to each other and to the chorionic vesicle as in the fourth week. Minot (*Human Embryology*, p. 13, 1892) describes the decidua serotina in a specimen of about this age (fifth week) as consisting of a compact and a spongy layer, the former constituting one quarter of the whole thickness of the serotina. The surface was without any trace of epithelium, but was covered with a thin fibrous and granular coagulum. The compact layer consisted almost exclusively of young large decidual cells and a clear homogeneous matrix; the cells were irregular in shape, but more or less rounded, with processes which occasionally united two cells together. In the deeper or spongy (cavernous) layer the decidual cells were not so large; they were more fusiform in shape, and had longer, less round nuclei. The spaces of the cavernous layer were glandular, and in many of them the shed epithelium (often degenerated) could be seen lying. In the smaller spaces the epithelium (columnar in type) was well preserved and still attached to the walls. The blood vessels lay between the glands, and Minot found nothing corresponding to the "colossal capillaries" of Turner.

The chorionic vesicle is still covered all over with villi, but these are most marked in the region corresponding to the decidua serotina. The minute anatomy of the parts is the same as in the fourth week. The space between the amniotic sac and the inner aspect of the chorionic vesicle—the extra-embryonic cœlom—is still large, but not so large as in the preceding week; at the end of the fifth week it may be stated roughly that the space between the embryo and the chorion is divided equally between the amniotic cavity and the cœlom (Mall, *Journ. Morphol.*, xii. 375, 1897). The amniotic membrane is still not far removed from the body of the embryo, and possesses the same histological appearances as formerly. The umbilical vesicle is pear-shaped; its stalk has lengthened considerably, and for the first part of its course is enclosed within the Bauchstiel; and the vesicle is no longer increasing in size.

The Embryo in the Fifth Week.

Various human embryos of the age of the fifth week have been described, several by His (Pr, M, Br, Rg, Ko, Sch, etc.), some by Minot and Coste, and others by Rabl, Phisalix, R. Dorello, and Hochstetter. In length the embryo now measures from 8 to 14 mm.; probably, then, 1 cm. may be taken as representing its average length about the middle of the fifth week. The distinct C shape of the fourth week is beginning to be partly lost: the body of the embryo shows some straightening, and so the head seems as if it formed a right angle with it. Between the region of the hind-brain and the back opposite the origin of the anterior limb-bud, there is a slight concavity, called *Nackengrube* by His; this persists till the eighth week (*vide* this Manual, vol. i. p. 81, 1902). Towards the end of the fifth week the head, as seen from the side, has an area about equal to that of the rest of the body; the cephalic and cervical flexures or bends are well marked, the latter reaching its maximum at this date. Both the Bauchstiel and the stalk of the umbilical vesicle have lengthened; they are combined in part of their extent to form the single structure, which may now be called the umbilical cord: towards the end of the week the cord shows one or two spiral turns, and contains one or more coils of intestine. The stalk of the umbilical vesicle is longer than the cord, and is disposed between the chorion and the amnion.

The limb-buds show a marked development during this period of seven days: at first they are unsegmented; then they exhibit two segments; then the tripartite division; and finally the digits are roughly indicated in outline, being still webbed. The upper limbs are generally more advanced in formation than the lower ones; for instance, they show digitation earlier. Along with their differentiation into three parts or segments, the limbs have undergone increase in size, and in embryos of about thirty-five days they project beyond the outline of the body in profile views. When the limbs are in the two-segment stage, the distal part is flattened and the proximal cylindrical, and there is a constriction between; later, a second furrow or constriction appears in the cylindrical part, dividing it into two parts. So the foot, leg, and thigh, and the hand, forearm, and arm are marked out.

The tail of the embryo is now very marked; in fact, in this (the fifth) week it reaches its maximum development, and is evidently a true tail (Fig. 17). At the other end of the embryo the cervical or præcervical sinus has greatly deepened, so that the fourth, third, and even the second branchial grooves have disappeared from the surface and lie within it. The first branchial groove is still seen; in fact it never enters into the cervical sinus, but persists externally as the external auditory meatus. Around it the six tubercles, which unite later to form the pinna or external ear, are quite recognisable. In the adjacent facial region marked changes can also be seen. The nasal pits are in process of demarcation by the growth of processes in the following manner: from the naso-frontal process its two lateral edges, the two globular processes as they are called, become thick and rounded, and form the inner boundaries of the nasal pits; and from the sides of the base of the naso-frontal process the two lateral nasal or frontal processes grow downwards and outwards, and bound the nasal pits externally, shutting them off from the depressions for the eyes. The nasal pits, however, are still in communication below with the primitive oral cavity. The lateral nasal process on each side is at first separated from the maxillary process of the same side by a groove (the naso-optic furrow or lachrymal groove), but later it unites with it and grows inward towards the middle line below the nasal pit; in the sixth week, as we shall see, it joins the naso-frontal process, and so separates the nasal pit from the oral cavity. Towards the end of the fifth week the mandibular processes unite in the middle line. About this time the optic vesicle comes into contact with the lens vesicle and is invaginated by it, becoming the secondary optic cup. The under surface of the vesicle is also invaginated, and so is that of its tubular stalk, so that an aperture (choroidal fissure) and a trough are thus formed. Mesodermic tissue grows into the optic cup through the choroidal fissure, and it also grows into the trough of the stalk (future optic nerve); in these places it gives origin later to the vitreous body and the central artery of the retina.

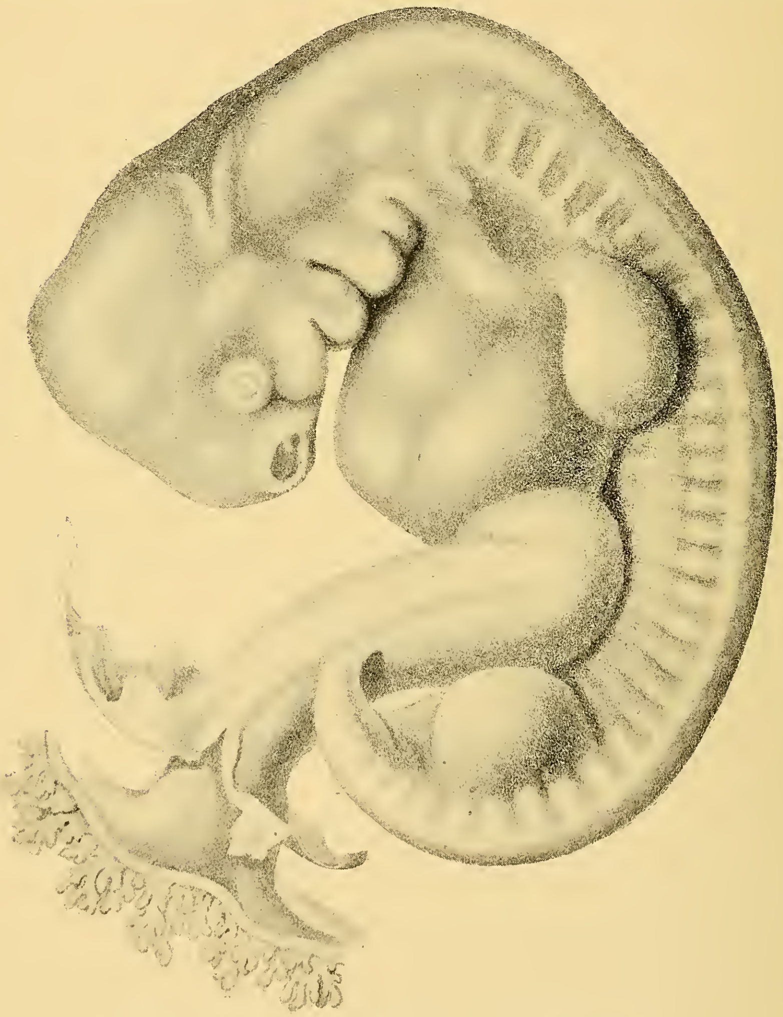

Fig. 17.—Embryo of the fifth week. Enlarged 15 times.
Embryo Pr. (After His.)

The only other external feature of note at this stage of development is the forward projection of the abdomen, due to the large size which the liver has now attained. It may be added that the ectoderm (or epiblast) covering the body consists of two layers: an outer one, the epitrichium, made up of slightly flattened cells which later become dome-shaped, and an inner layer of larger cells which give rise to the epidermis.

The internal arrangements may now be described, the same order of description being followed as was adopted for the fourth week.

The spinal cord, in the fifth week, is divisible into three layers: an outer neuroglia layer or marginal velum, a middle or mantle layer, and an inner or ependymal layer. These have increased in thickness, and the cells of the ependyma have become ciliated. The sympathetic system shows a further advance in formation. Two ganglionic masses are found near the omphalo-mesenteric artery, one above and the other below the vessel; these represent the ganglia of the solar plexus, and the upper ganglion is joined to the ganglionated cord by fibres representing the greater and lesser splanchnic nerves. Near the origin of the umbilical arteries is another enlargement of the ganglionated cord, which represents the pelvic plexus (inferior mesenteric and hypogastric ganglia). Cells, also, are found in the neighbourhood of the stomach, and these are connected with a plexus formed from fibres from the vagus nerves. In the cervical region a plexus is being formed, composed of ganglia of cells which have wandered from the cell column and of fibres closely related with the descending branches of the vagus.

In the brain, changes are manifest. A longitudinal ridge-like thickening appears in the roof or dorsal wall of the *mid-brain vesicle* or mesencephalon; later, in the ninth week, this is replaced by a furrow, at the sides of which are developed the corpora quadrigemina, but as yet there is no trace of these bodies. In the *hind-brain* or rhombencephalon, further developments are visible now both in the floor and in the roof. The roof-plate is wide and thin; over the posterior half of the fourth ventricle it forms the inferior medullary velum, while over the anterior half the superior medullary velum develops as well as the rudiment of the cerebellum. Out of the alar and basal laminæ are formed the rudiments of the pons and medulla; the attachments of the roof-plate or velum to the alar laminæ is marked by the obex and ligula, which are thickenings on the margins of the lower angle of the fourth ventricle. The rudiment of the restiform body is found in the upper margin of the alar lamina. If we now look at the parts in front of the mesencephalon, we find that the roof-plate of the *diencephalon* or inter-brain is thin-walled and somewhat folded, while in the floor-plate is a well-marked ventral groove; the lateral walls are divided into dorsal and ventral zones by the grooves known as the sulci of Monro, which extend forward towards the point of origin of the optic evaginations. At the posterior end of the folded roof-plate is an elevation which later becomes a hollow evagination, the pineal process, and still later the pineal body or epiphysis. The rest of the roof-plate in front of the pineal elevation represents the velum interpositum of adult anatomy; it forms a ridge at first, but soon becomes a thin membrane upon which at a later date blood vessels arrange themselves, and the whole structure is invaginated into the third ventricle as the choroid plexus. The dorsal zones of the lateral walls thicken, and towards the end of the fifth week begin to project inwards into the cavity of the ventricle as the optic thalami. Behind the optic thalami are other thickenings giving rise to the pulvinares and the external geniculate bodies. The ventral zones become the subthalamic regions, and in them or perhaps in the floor-plate are developed the corpora albicantia (mammillary tubercles). In front of the diencephalon is the *telencephalon* or hemisphere-brain. It has, as we have already seen in the end of the fourth week, a median portion which contains the anterior part of the third ventricle, and two lateral outgrowths, the cerebral hemispheres. The roof of the median portion is converted into the anterior part of the velum interpositum. From its dorsal zones arise the optic evaginations, as has already been pointed out; while the ventral zones form the anterior part of the subthalamic regions. In the floor-plate is the evagination of the hypophysis which during this week comes into contact with the invagination of the roof of the oral cavity to form with it the pituitary body. The cerebral hemispheres arise from the sides of the dorsal zones, and also get a prolongation of the roof-plate or velum interpositum. In the ventral part of the wall of each a thickening is to be noted, the future corpus striatum, and in the more dorsal part is the mantle or pallial portion of the hemisphere. The cavities of the hemispheres are, of course, the lateral ventricles, and into them project the choroidal folds which do not at this date possess blood vessels. In this relation are to be observed the arcuate and choroidal fissures. In the floor of the telencephalon the tuber cinereum appears. The first indication of the falx cerebri is found lying in the longitudinal fissure between the two cerebral hemispheres. There are as yet no traces of the corpus callosum or fornix. The olfactory lobes can now be recognised as areas on the ventral surface of the cerebral hemispheres; they are at first hollow and later become solid, and finally (third month) give rise to the olfactory bulbs and stalks and to the olfactory tracts, trigone, and anterior perforated spaces.

The origins of the cranial nerves as they exist in the fourth week have been already sketched; but some further developments may here be noted. During the fifth week the olfactory nerves are much more distinctly indicated than in the preceding week; the olfactory ganglion is produced, its cells assume the bipolar form, and by the elongation of their poles on the one side they come into relation with the brain, while on the other side they join the olfactory epithelium. In His' embryo Ko (a fifth week specimen), the ganglia and trunks of the third (oculo-motor), fourth (trochlear), fifth (trigeminus), seventh (facial), eighth (acoustic), ninth (glosso-pharyngeal), tenth (vagus), eleventh (spinal-accessory), and twelfth (hypoglossal) nerves can all be much more clearly traced than in fourth week embryos. The sixth (abducens) nerve is composed entirely of fibres arising in the ventral or basal zone of the hind-brain; it has no ganglion. The eighth nerve has a vestibular and a cochlear branch; at this time the ear has advanced in development, the semicircular canals have commenced to form, and the twisting of the cochlea has begun. The eleventh nerve and its branches have practically their adult relations in this week of embryonic life, and the twelfth (hypoglossal) nerve passes round the sinus cervicalis and then curves forward into the tongue.

The alimentary system, in the fifth week, shows some increase in complexity. The oral cavity is not yet shut off from the nasal. The front of the tongue is marked off from the back by two oblique lines which begin at the foramen cæcum and form an open V; the anterior part is developed from the tuberculum impar, and the posterior from the region of the second and third branchial arches (ventral ends). At the opening (the future foramen cæcum) is the orifice of the duct of the median part of the thyroid gland (thyroglossal duct); it loses its lumen and begins to atrophy at the fifth week. Towards the end of the week a longitudinal ridge appears on each side in the floor of the mouth in the part known as the alveolo-lingual groove; this is the *anlage* of the submaxillary gland and Wharton's duct. The pharynx is still relatively large, being equal to about half the length of the alimentary canal. The pharyngeal pouches are beginning to undergo the series of changes which transform them into permanent structures; for example, the first pouch, on each side, is being shut off to form the tympanic cavity at one end and the future Eustachian tube at the other, the "closing membrane" persisting as the tympanum; the median lobe of the thyroid gland is related to the anterior ends of the second pair of pouches; and from each of the two fourth pouches arises a ventral prolongation or diverticulum, which becomes the *anlage* of one of the two lateral lobes of the thyroid gland. At a later date (sixth week) evaginations from the third pair of pockets give origin to the epithelial parts of the thymus gland.

The opening of the trachea into the pharynx is slit-like; in front is the *anlage* of the epiglottis, and at the sides are the arytenoid ridges whose thickened epithelium almost closes the opening; in the ridges, on each side, are two projections, the cuneiform and cornicular tubercles. There are as yet no traces of the cartilages of the larynx; these appear at the seventh week, and the cartilages of the trachea a week or two later. Through an increase in the number and size of their lobes the lungs become much more than simple buds. A pulmonary artery can be traced to each of them.

To return, now, to the description of the alimentary system, it may be observed that during the fifth week the noteworthy flexure of the intestine below the level of the stomach is established. In this way is formed a U-shaped loop, with its closed end projecting towards the ventral body-wall; the dorsal mesentery at this point lengthens in order to permit of this formation. The vitelline duct or yolk-stalk is attached to the apex of the U-shaped loop, and may remain permanently as Meckel's diverticulum; the vitelline artery (superior mesenteric) supplies the loop. At a point on the lower border of the loop the intestine suddenly becomes larger; this indicates the caput cæcum or commencement of the large intestine. All the bowel above this point forms the small intestine, and thus it comes about that Meckel's diverticulum, when present, is attached to the ileum above the level of the ileo-cæcal valve. At first the U-shaped loop is extra-abdominal in position, being situated in a cavity formed by the somatopleure at the umbilicus; as a rule, it passes within the abdomen by the end of the second month. The angle between the U-shaped loop and the hind-gut becomes the splenic flexure, although as yet, of course, there is no trace of the *anlage* of the spleen. The hind-gut is supplied with a dorsal mesentery by which it is suspended. The inner surface of the intestine is as yet quite smooth, folds not making their appearance till the next week. It has been stated that towards the end of the fifth week the mucous membrane of the duodenum increases so much in thickness that the lumen is narrowed and finally obliterated, to reappear again at the beginning of the sixth week (Tandler). The pancreas lies between the layers of the dorsal meso-gastrium at this age, and is parallel to the greater curvature of the stomach. The part of the dorsal meso-gastrium which lies between the pancreas and the stomach becomes at a later date much elongated, to form the great omentum. The liver develops rapidly during this week, increasing greatly in size, and causing the anterior abdominal wall to project, as may be well seen in Mall's reconstructed embryo No. ix. (*Johns Hopkins Hosp. Bull.*, ix. p. 199, 1898). The gall-bladder is quite recognisable in this embryo. During this week (the fifth) the end-gut (*pars ultima* of Berry Hart) is in course of disappearance. The entodermal cloaca (*pars penultima*) is now divided into an anterior and a posterior division, the former forming the bladder and urinogenital sinus, and the latter the rectum. In the sixth week both the bowel and urinogenital sinus communicate with a large space, the cloaca, best known as the ectodermal cloaca. It may be conjectured, for we do not know with certainty, that this cloaca has been formed during the fifth week by the breaking down of an ectodermic pyramidal plug with its apex towards the lower part of the urinogenital sinus meeting the coronal partition of the primitive gut (Berry Hart, *loc. cit.*). Apparently the communication of the cloaca with the exterior thus established becomes shut off again between the seventh and eighth weeks by Reichel's anal tuberosities (*Analhöcker*).

The urinogenital organs have advanced considerably in their ontogeny since the fourth week. The mesonephros or Wolffian body is still well developed and large. It extends as a ridge on each side of the spine from the posterior cervical region to the pelvis. To its inner side lies the genital ridge, and it is possible, according to Nagel (*Arch. f. mikrosk. Anat.*, xxxiv. 269, 1889), even at this age (fifth week) to determine by microscopical examination whether the genital gland is male or female; if it is to be an ovary the large germinal cells (primitive ova) are numerous, and the germinal or cœlomic epithelium forms a thick layer of several rows of cells, while if it is to be a testicle the large germinal cells are fewer, and the cells of the epithelium are arranged in groups rather than in a distinct band or layer. The convoluted tubules and glomeruli of the Wolffian bodies open into the Wolffian ducts, and these in their turn open into the entodermal cloaca. As has been already pointed out, the ureter is present at the end of the fourth week as a small bud attached to the Wolffian duct just above its opening into the cloaca; in the fifth week this bud develops a stalk and becomes the permanent kidney and duct (ureter) which lie in the lumbar region behind both the Wolffian body and the peritoneum. The permanent kidney or metanephros, then, is developed from this outgrowth from the Wolffian duct; at the same time it is believed that it obtains part of its structure from a condensation of the mesenchyma which surrounds it, to which the name of metanephric blastema has been given. Possibly the blastema only contributes the connective tissue and vessels of the kidney. About the end of the fifth week, or perhaps in the sixth week (the time is not known with certainty), the Müllerian ducts appear as peritoneal evaginations in the ridge or folds that lie on the ventral surface of the Wolffian bodies. The Müllerian ducts come to open into the urinogenital canal posteriorly, while anteriorly they have a free communication with the peritoneal cavity. A trace of the external genitals is visible during the fifth week in the shape of the genital tubercle, a small eminence on the ventral wall of the urinogenital sinus. At this time, also, the suprarenal capsules or bodies are quite recognisable, and each is found near the cephalic end of the mesonephros or Wolffian body of the same side. Their relation to the kidney is a later acquired one. They are probably derived from the Wolffian bodies; but a part (medulla) has origin in the sympathetic nervous system.

The heart and circulatory system are now well advanced in development. The auricles and ventricles are not yet fully separated into right and left chambers. The opening of the sinus venosus into the right auricle is guarded by right and left lateral valves, which prevent regurgitation of blood when the auricle contracts. At a later date the right valve becomes the Eustachian and Thebesian valves; probably the left forms part of the auricular septum (primary). Even as early as the fifth week a trace of the secondary septum (or septum spurium) of the auricles can be made out lying to the right of the primary one. The auriculo-ventricular canal is divided into right and left auriculo-ventricular orifices by two structures known as the anterior and posterior endocardial cushions. The bulbus arteriosus is divided into an anterior or pulmonary and a posterior or aortic part by anterior and posterior ridges (anterior and posterior aortic septa), which fuse together while their lower ends unite with the interventricular septum. The resulting aortic part retains its connection with the fourth left aortic arch, which becomes the ascending part of the arch of the aorta; the pulmonary or anterior part is continuous with the fifth arch of the left side and constitutes the ductus arteriosus (or ductus Botalli), with branches to the two lungs. It is not known how this change in the relations of the pulmonary arteries, so that both arise from the fifth left arch, is brought about (Minot). The fifth arch on the right side atrophies; the right fourth arch persists as the right subclavian and innominate arteries; the third arch on each side remains as the internal carotid. Now, therefore, the third and fourth arches and the vessels representing the first and second arches are all connected with the left side of the heart through the aorta, while the left fifth arch is brought into relation with the right ventricle through the pulmonary trunk. The segmental arteries and the vessels for the limbs doubtless undergo important modifications during this week, but these are not yet clearly known. The arrangement of the veins is probably similar to that described for the fourth week; the origin of the vena cava inferior has not yet been clearly ascertained for the human embryo. The blood at this age contains only nucleated red blood corpuscles or erythrocytes.

The sustentacular parts of the embryo show further developments at the fifth week. For instance, in the limbs the fibrous basis of some of the future bones can be recognised, and here and there chondrification has begun. In the pelvis, also, the three parts of the *anlage* of the os innominatum (ilium, ischium, pubes) are present; so are the membranous ribs and clavicle, etc. According to Arthur Thomson (Cunningham's *Text Book of Anatomy*, p. 180, 1902), ossification may be seen in the clavicle as early as the fifth week. Meckel's cartilage is present in the mandibular arch.

It must be admitted that there is much that is uncertain about human ontogenesis in the fifth week after impregnation. In this period take place several complicated rearrangements of parts; and just how these rearrangements are effected we do not clearly understand. This remark applies specially to the changes which occur in the branchial arches and clefts, in the pharyngeal pouches, in the great veins of the abdomen and liver, and in the pleuro-peritoneal relations. We do not know how these changes take place, neither do we know with any degree of certainty when they occur. Consequently any attempt to place before the reader a chronological account of the embryology of this period has to face the double difficulty of uncertainty as to the facts and ignorance regarding the dates. There is also the constant problem of the recognition of parts; for when one, so to say, loses sight of a structure in the embryo for a day or two it is not easy to recognise it again at a later stage in a new form and with new relations. The whole problem, therefore, becomes a very complex, involved, intricate, and perplexing one; yet, in order to preserve unbroken the chronological account of human embryonic life, I felt myself constrained to put before my readers such facts as I could gather together from reliable authorities. They are few in number and obscure, but they must serve till further light has been thrown upon this feebly illumined part of ontogenesis. In may be said, in parenthesis, that the nomenclature of embryology does nothing to render this obscure portion of the subject less dark; in fact, the giving of two, three, or even four different names to the same structure is irritatingly confusing.

Although there is much that is obscure about organogenesis in the fifth week there is also not a little that is well known. The embryo begins to lose something of the exaggerated C shape that it had in the preceding week, and attains to the length of 1 cm., being now about one-fiftieth of the length of the mature fœtus. Much has yet to be accomplished before the 1 cm. embryo is converted into the 51 cm. fœtus, but it may be doubted whether any of the superadded centimetres are accompanied by such a marvellous exhibition of developmental activity as is this first one. Among the many phenomena of the week we must note the assumption by the Bauchstiel and yolk-stalk of a truly cord-like character, the transformation of the bud-like extremities into evident and segmented limbs, and the presence of a decided and indisputable tail. The face is now more face-like, having a lower jaw united in the middle line, nasal pits which, although incomplete, suggest a nose, and recognisable eyes but with no eyelids or even *anlages* of eyelids. The embryo is beginning to be dimly human in appearance, a change which is aided by the disappearance of the second, third, and fourth branchial arches and grooves into the sinus præcervicalis whose margins close over and entomb them.

In its internal arrangements the embryo is rapidly passing towards a more mature distribution of structures and organs. The origins of cranial nerves can be recognised; the pituitary body is present, so are suprarenal capsules and a sympathetic system with a solar plexus; the bowel has thrown itself into a U-shaped loop, and given thus an indication of its coming division into small and large intestine; the thyroglossal duct is beginning to close; the ureters are present as little buds from the Wolffian ducts; and in the genital ridges histological evidence can be obtained of the sex to which the embryo belongs. In the region of the brain, also, the *anlages* of numbers of new parts and structures have appeared, including those of the medullary velum, pons, velum interpositum, optic thalami, corpora striata, tuber cinereum, and falx cerebri. Finally, the surface of the whole body is covered by the epitrichium, that mysterious layer whose fate and whose functions are alike unknown.

CHAPTER VI

Chronology of Embryonic Life (*continued*): Conditions found in the Sixth Week after Impregnation.

The sixth week after impregnation is the last of typically embryonic life. It is not that there is no further organogenesis after this period, as a matter of fact some organogenesis is going on up to the full term of antenatal existence and even after it; but the sixth week marks the close of the epoch of almost purely constructive processes. By this time all the great formative procedures have been initiated; the plan of the human embryo has been, as it were, fully indicated; some complicated rearrangements have also been effected; and the embryo may now be called the transition-organism, for although it is not yet a fœtus it is no longer simply an embryo. We may call it the neo-fœtus. There is still much to be done: many of the organogenetic processes have to be carried to completion; a great deal of histological differentiation has to be effected; many parts have yet to assume their mature relations with each other and with the framework of the body; the organism has to grow from an embryo measuring little more than half an inch in length to a fœtus of twenty inches; and modifications have to occur in the manner in which its organs carry on their functions, and in the relations which they bear to the maternal economy. Nevertheless, for the organism as a whole, truly embryonic life has nearly finished; and what remains to be done is no longer development but growth and histological and physiological differentiation. I have already in the part of this MANUAL dealing with the Fœtus described the characters of the embryo at the close of the sixth week. It is not, therefore, necessary for me to repeat the whole of that description here. I take the opportunity, however, of giving in greater detail some obscure parts of the subject, and of adding some information only recently made available by the progress of embryological research. It has, for instance, been found that the *anlages* of certain structures are present at an earlier date than had been thought. These facts and others of the same kind are noted here. Let us, with these words of explanation, proceed to the study of the organogenetic processes of the sixth week.

Extra-embryonic Parts in the Sixth Week.

J. C. Webster gives a good and detailed account of the extra-embryonic parts of the uterine contents at the sixth week (*Human Placen-*

tation, pp. 15, 28, 38, etc., 1901); upon this the following description is based.

The decidua vera varies from 3 to 7 mm. in thickness, and can be readily divided into a compact and a spongy layer. The spongy part can be subdivided into an outer part with slightly branched glands, and a deeper portion where there is much branching. The lining epithelium is still to a great extent present, although somewhat altered: the columnar cells are now cubical or flattened; their nuclei are rounded or flattened in shape, and some have degenerated; and the cilia have disappeared. The glands have increased in size, but there is no complete evidence of any new formation of them; their mouths (in the compact layer) are narrowed or obliterated; their deeper parts are much enlarged; their epithelium is generally cubical or flattened, very rarely columnar, and in many instances is shed in masses or in individual cells. In the interglandular tissue the most marked change is the development of the decidual cells: this change is practically limited at present to the compact layer, and is most evident in its outer portion; the decidual cells are rounded, oval, polygonal, or spindle-shaped, with large and somewhat rounded nuclei, and in most places they are connected by broad or slender processes; and here and there they are seen with two nuclei, probably indicating the occurrence of cell-division. In the compact layer the capillaries in some parts are enormously dilated, in other parts there is only a moderate increase in size; here and there are small extravasations of blood in the decidual tissue.

The decidua reflexa (capsularis) has not yet come into contact with the vera, so that a uterine cavity still exists, although it is diminished in size by the growth of the embryo and its envelopes. The basal and polar part of the reflexa can be distinguished: the former consists of an inner compact and an outer spongy layer which contains gland spaces, not so numerous as in the corresponding layer of the vera or serotina; the latter or polar portion contains very few or no glands. None of the glands open on the inner surface of the reflexa. Blood spaces are to be seen throughout the membrane; in the basal part some communicate with the intervillous spaces of the opposed chorion læve; and here and there masses of syncytium may be traced into the vessels. At this age there are already signs of degeneration in the reflexa, of the nature of coagulation-necrosis of the decidual tissue, so that in the innermost part is found a layer of fibrin-like material thickest at the pole. Possibly some of the fibrin may arise from the blood. On the inner surface of the reflexa no trace of maternal epithelial cells can be seen, and on the outer surface is an epithelium with much the same characters as that on the vera (cubical or flattened, not ciliated).

The decidua serotina is from 2 to 3 mm. in thickness, and the compact layer measures about one-quarter of the whole. In some parts the whole decidua looks as if made up of the compact layer, but as Webster points out this may be a variation of no importance. The surface is irregular and no surface epithelium is visible. The outer parts of the glands in the compact layer are obliterated, and both in them and in the deeper parts in the spongy layer the lining epithelium may be cubical or irregular, attached or loose, and more or less degenerated. In the interglandular tissue characteristic decidual cells are found in some parts, and in others they show signs of degeneration. The superficial part of the compacta shows an irregular layer of fibrin-like material; this has to be distinguished from the layer of fibrin on the surface which results from coagulation of the blood. At intervals chorionic villi are fixed to the surface, and between them flattened masses of protoplasm (syncytium or plasmodium) are attached. The syncytium forms a more broken layer than it did before. There are no cell outlines, and the nuclei are arranged either in rows or quite irregularly. Here and there the masses of syncytium are thickened and resemble very large multinucleated giant cells, with prolongations running into the intervillous spaces. It is to be noted that no structure at all like this is to be found on the surface of the decidua vera, one among several reasons which lead us to believe that it is of fœtal origin. Processes of it extend into the substance of the decidua as deep as the muscular coat. In the spongy layer of the serotina are numerous small tortuous arteries; in the compact layer the arteries cannot be distinguished from the veins; there are numerous sinuses which may be dilated capillaries, and some of them can be seen to open into intervillous spaces and to contain masses of syncytium attached to the wall.

The surface of the chorion which is opposed to the decidua serotina is thickly covered with much branched villi. They show a thick layer of syncytium and a comparatively thin underlying cellular layer. Both on the general chorionic surface and on the villi are little projections of the syncytium. The mesoblast of the chorion and that which forms the cores of the villi has a denser and a more fibrillated appearance than in the earlier weeks, and here and there it forms a sort of basement membrane under the cellular or Langhans' layer. In the smaller villi the mesoblast is of a mucoid type; and capillaries exist in most of them, whether small or large. Among the villi are irregularly shaped pieces of syncytium, and clumps of decidual cells with pieces of Langhans' layer attached to them. The decidual masses may show signs of fibrinous or hyaline degeneration. The attachment of the villi to the serotina seems to be by means of the proliferated mass of cells of Langhans' layer at the tips; apparently the syncytium has nothing to do with it. The villi are attached at no regular intervals, by a main stem or by branches, and at right angles or obliquely to the surface. From the chorionic surface which is opposed to the decidua reflexa not nearly so many villi spring; they are less branched, show very few bud-like projections, are poorly supplied with capillaries, and sometimes contain connective tissue which is swollen or hyaline.

From the foregoing description it will be learned that the decidual and chorionic investments of the embryo have not altered greatly from what existed in the two preceding weeks. The space, however, between the vera and reflexa is much smaller, and the reflexa already has begun to show retrogressive changes. The glands, also, of all the decidual membranes are in a more or less marked state of degeneration; this is true even of the serotina, in which, however, the other parts are as yet in full activity. There is a still further development of the chorion and its villi opposed to the decidua serotina; and, although there is not here a separate and recognisable placenta, there is the physiological equivalent of that organ. The important part played by the fœtal tissues in the construction of the placenta is also quite apparent.

The amniotic sac has now increased with the marked growth of the embryo, so that the space (extra-embryonic cœlom) between it and the inner surface of the chorionic vesicle has practically disappeared. The histological characters of the membrane scarcely alter, but the matrix between its two layers becomes somewhat condensed and fibrillated. The yolk-sac or umbilical vesicle has much the same size as in the fourth week; it is obviously being left behind by the embryo in the progress of ontogenesis, for its useful part is played already. Consequently the vitelline circulation is atrophying. The great characteristics of the extra-embryonic structures in the sixth week are the growing importance of the chorionic villi which face the decidua serotina, with the consequent establishment ere long of a true and anatomically recognisable placenta, and the dwindling of the decidua reflexa and umbilical vesicle. One of the great rearrangements of ontogenesis is in progress. By its means intrauterine existence is to be prolonged for seven months or more.

The Embryo in the Sixth Week.

The embryo at the sixth week measures from 14 to 17 or 18 mm. in length. The increase in length during this and the preceding week is in part due to the straightening of the body and the raising of the head. The changes in the external appearances of the embryo are also largely caused by this alteration in attitude. The neck bend becomes in consequence more rectangular, and the concavity at the back of the neck (*Nackengrube*) less marked. The mid-brain comes to lie more directly above the hind-brain. The abdomen is still more prominent than it was in the fifth week, with the result that the limbs do not in profile views reach to the outline of it. Other external features at this age are: the presence of a distinct tail, which, however, is relatively smaller than before; the indication towards the end of the week of slight folds surrounding the conjunctival area, the *anlages* of the future eyelids; the appearance of the fingers as separate outgrowths; the existence of a recognisable external ear or concha; the completion of the upper part of the face by the union of the two maxillary processes; and the direction of the long axes of the limbs at right angles to that of the body. The umbilical cord is now quite distinct in its whole length, and still evidently contains a loop of intestine.

If we look more closely at the face at this period of embryonic life, we shall see that through the union of the maxillary processes with the lateral nasal and fronto-nasal processes the external boundaries of the nostrils have been marked out and the mouth cavity shut off from the nasal pits. There is consequently a recognisable but very broad nose, the nasal pits being the anterior nares. It is noteworthy, also, that through the downward growth of the fronto-nasal process the mouth receives a new upper boundary. Posterior to this process the oral and nasal cavities freely communicate, for the two lateral halves of the palate do not begin to unite till the eighth week. The oral surface of the upper jaw already (towards the end of the sixth week) shows two parallel ridges, which afterwards become the upper lip and the gum. At the posterior end of the embryo the genital tubercle is now clearly recognisable; behind it is the cloacal fossa, and encircling the fossa is a ridge (genital ridge of the external genitals); no groove has yet appeared on the under surface of the genital tubercle. The histological examination of the skin shows the same two layers as in the fifth week with an indication of the dermis or cutis beneath them.

There are no very radical changes to be noted in the internal conditions of the embryo in this week. As has been already stated, most of the embryonic rearrangements have been initiated and many of them have been almost carried through. Such changes as there are affect specially the brain and spinal cord, the ear and eye, the genito-urinary organs, and the sustentacular framework of the body.

The alterations in the spinal cord are evident. The central canal has changed from an oval running antero-posteriorly into a somewhat rhomboidal form. The lateral angles of the lozenge-shaped space thus produced divide the lateral walls very distinctly into two zones or laminæ, an alar or dorsal and a basal or ventral. The roof- and floor-plates (mid-dorsal and mid-ventral laminæ) show no changes; but the alar and basal laminæ of the lateral walls do so. The posterior nerve-roots, of which there were indications at the fourth and fifth weeks, can now be recognised passing into the alar lamina; while the anterior or ventral roots take origin in the ventral lamina. At present the cells of the ventral zone are much more numerous than those of the dorsal, so that the rudiment of the anterior horn of grey matter is much larger than that of the posterior horn. There is also some sign of the developing white columns of the cord: the grey matter of the anterior horn is separated from the ventral surface of the cord by a zone in which longitudinal nerve fibres are found, the commencing anterior white column; in a less marked fashion the posterior white columns have begun to be evident between the posterior horn and the surface. There is, as yet, little or no trace of lateral columns, and there are no signs of an anterior or a posterior fissure. About this time the two ventral arteries unite into a single median vessel (arteria sulci). The whole of the complicated arrangement of bundles of fibres in the cord comes into being later than the sixth week, that is to say in the fœtal and not in the embryonic period of antenatal life.

The changes in the brain are of the nature of continuations of those initiated in the fifth week, and the reader may refer to the preceding chapter for the account of them. There are some slight indications of further structural elaborations to which an allusion may be made. In the hind-brain or rhombencephalon and in that part of it (myelencephalon) which becomes the medulla oblongata, there is a broadening out of both roof-plate and dorsal part of the brain cavity so that the margins of the dorsal zone or alar lamina have a lateral position and are bent towards the ventral aspect to form a reflected lip (*Rautenlippe*). In the sixth week this lip continues to grow towards the ventral aspect of the myelencephalon to which it is united, and it thus buries parts (*e.g.* tractus solitarius) which primarily lay on the surface. Through this bending, the surfaces of the dorsal zone come to be dorsal and ventral instead of internal and external; from it the future restiform body is formed. The ventral zones show marked thickening, and so the floor of the cavity of the myelencephalon (fourth ventricle) is flattened. The grey matter of the ventral zones forms the formatio reticularis; it is surrounded by great numbers of neuroblasts (future olivary bodies, etc.). Probably somewhat similar changes occur in the metencephalon and mesencephalon. The form and divisions of the diencephalon, as described under the fifth week, are maintained; the pineal body or epiphysis, a product of the roof-plate, is now more evident; there is also an expansion of the subthalamic regions, which probably are the continuations forward of the formatio reticularis. In the telencephalon, the lamina terminalis, to which reference has already been made and which probably represents the roof-plate of this part of the brain, becomes thickened and constitutes the *anlage* of the septum lucidum, the corpus callosum, the fornix, and the anterior commissure. It is not till much later that a cavity forms in the septum lucidum, to be known as the fifth ventricle. The cerebral hemispheres are now growing rapidly and project forwards and upwards in front of the diencephalon; their communications with the third ventricle (foramina of Monro) do not enlarge but their walls thicken, and therefore the connecting structures enlarge; a commencement of the delimitation of the hemispheres into lobes is effected by the development of the fossa of Sylvius which marks off a frontal lobe and a post-

Sylvian lobe (future temporal and occipital lobes), each of which contains part of the lateral ventricle. About the sixth week the olfactory ganglion on each side unites with the bulbus olfactorius of the olfactory lobe of that side.

With regard to the eye, it may be noted that in this or in the succeeding week (the seventh) the choroidal fissure disappears by a fusion of its lips. The ocular tunics also begin to form; thus mesodermic tissue surrounds the lens-vesicle and constitutes the tunica vasculosa lentis. In this tunic, vessels are developed which are associated with the hyaloid artery of the vitreous humour. The position of the eye changes: at first it was lateral and high up; in the fifth week it descended somewhat; and, now, in the sixth week it moves round more to the front; but even at the end of the second month the axes of the two eyes are far from parallel. In the middle ear the malleus and incus and their relations with Meckel's cartilage can be recognised; the cartilage of the second branchial arch is also present with the seventh nerve close behind its posterior end, and with a ring of cartilage above it, representing the stapes. The internal ear shows a differentiation into semicircular canals, cochlea, endolymphatic duct, sacculus, and utricle. From six tubercles and a ridge lying posterior to them the external ear (pinna or concha) is taking form. One tubercle becomes the future tragus, another the antitragus, another the lobule, another the antihelix, and the two remaining ones along with the ridge become the helix.

The alimentary system, like the nervous, shows no marked new developments during this week; in fact, with the exception of the development of the rectum, anus, and perineum, and the rearrangement of the intestinal coils, this part of the body of the embryo may be said to have taken on its permanent form. In the mouth the *anlage* of the submaxillary gland is now more evident than it was in the fifth week; and traces of the *anlages* of the parotid and sublingual glands may perhaps have appeared. The dental shelf is visible as a horizontal outgrowth from the epithelial downgrowth which gives rise to the lip groove. In the third pair of pharyngeal pouches the epithelial part of the thymus gland is beginning to form. There is as yet no trace of the tonsils. The œsophagus is relatively longer than before, and the stomach shows more distinctly its greater and lesser curvatures. The duodenum is clearly marked off as the part of small intestine which passes from the pyloric end of the stomach towards the dorsal body-wall. Below this is the U-shaped loop already described with the indication of the cæcum. About this time the lower limb of the U so alters its position that it comes to lie above the upper limb, and thus the cæcum, transverse colon, and descending colon come to occupy their adult relations to the small intestines. The descent of the cæcum and the development of the ascending colon, however, have yet to take place. Five other primary coils of the small intestine, in addition to the duodenal one, can be recognised; all these five lie within the umbilical cord at present (Mall, *Johns Hopkins Hosp. Bull.*, ix. 197, 1898). The ectodermal cloaca is now present, but of this more must be said in the next paragraph.

Into the ectodermal cloaca open the urino-genital sinus and the bowel. The bowel, however, which opens into the cloaca does not apparently constitute the permanent anus. The cloaca, it would seem, is closed again, and the perineum formed by the growth of two eminences (Reichel's *Analhöcker*) at the sides of it. In the present week it communicates with the exterior, and into it opens the urino-genital sinus. The Wolffian ducts in turn open into the urino-genital sinus. The two Müllerian ducts can be recognised at this age; they lie in the genital cord along with the Wolffian ducts, and have apparently in part coalesced into one duct (Berry Hart, *Trans. Edinb. Obst. Soc.*, xxvi. 264, 1901); in the upper part of their course they are separate. The kidneys and ureters are present; the latter have as yet no connection with the bladder. The Wolffian bodies may even now show signs of regression.

Little need be said regarding the respiratory and circulatory systems in this week of embryonic life. The larynx is recognisable as the dilated part of the trachea which opens into the pharynx; and the arytenoid ridges are better marked than in the preceding week. In the heart the interventricular septum, the endocardial cushions, and the aortic ridges meet and are united by a thin membrane, the pars membranacea septi; thus the ventricles are separated. The sustentacular system shows marked progress; if the clavicle has not yet begun to ossify, it may show signs of doing so now; ossification begins also in the lower jaw around Meckel's cartilage; the ribs and basis cranii are undergoing chondrification; and cartilage is evident in the bodies of the vertebræ. According to some authorities the *anlage* of the spleen may be seen even at the fifth week as a thickening of the mesoderm (mesenchyma) on the dorsal surface of the mesogastrium; according to others it is not recognisable till the eighth week.

The sixth week is, as has been stated already, the closing period of purely embryonic life. We expect, therefore, to find in it some slackening in the rate of development, and some diminution in the variety of organogenetic processes. There are fewer surprises of evolution; and there is a greater tendency for the constructive procedures to follow in their progression the lines that have been already indicated. The period of rapid transformations and of bewildering rearrangements and alterations is past.

In the extra-embryonic parts it is evident that the typically decidual environment has reached the culminating point of its functional importance and usefulness; already there are abundant signs that in future it is to be one part only of the caducal membranes (the decidua serotina) that is to pursue the path of elaboration and structural differentiation, while the others follow retrogressive ways. The preponderating importance of the chorionic villi of the chorion frondosum is becoming more and more evident, while the dwindling of the umbilical vesicle, its attachments, and its circulation is clearly recognisable. The *placenta* looms big in the immediate future of antenatal affairs. There has also been so marked an expansion of the amniotic sac and its contents (liquor amnii and embryo) that its walls are now close to those of the chorionic vesicle and the extra-embryonic cœlom has disappeared.

The embryo has lost a little more of its exaggerated C shape; its abdomen has become more prominent and its tail less so; it has recognisably separate fingers, although its toes are not so far advanced; the mouth and nose are shut off from each other externally, and so there is a face; the eyes are coming round more to the front; the tubercles which go to form the external ear or pinna are grouping themselves so as to shadow forth that structure; and, at the other end of the body, the genital tubercle, which is later to give origin to the penis or the clitoris, is recognisable. By an organogenetic rearrangement, the details of which are unknown to us, the entodermal cloaca has become transformed into the bladder and other parts, and an ectodermal cloaca open to the exterior has appeared.

In the embryonic interior some further differentiations are in progress. The *anlages* of the salivary glands, the thymus, the larynx, the kidneys, and perhaps the spleen have appeared; the complicated changes (possibly including ossification) which lead to the disappearance of Meckel's cartilage and the formation of the auditory ossicles have begun, and ossification has commenced in the clavicle. The intestinal coils have made their great rotation with resulting complexity of arrangement of themselves and of their mesentery. The spinal cord begins to show traces of its mature division into grey and white matter, or at least into the *anlages* of the grey horns and of the white columns; and the posterior roots of the spinal nerves are forming. In the brain the signs of the great hemispherical expansion are still more evident than in the preceding week; the fossa of Sylvius with its adumbration of innumerable fissures and convolutions yet to be evolved is to be recognised; and the pineal body and the *anlage* of the corpus callosum are present.

Organogenetic Rearrangements.

Before I pass from this brief sketch of development during the embryonic period (it is, as I have already pointed out, nothing more than a sketch), it may be well if I recapitulate shortly some of the more complicated organogenetic rearrangements. The chronological method does not lend itself to the description of intricate phenomena of ontogenesis extending over prolonged periods, hence the necessity of recapitulation and grouping. The embryological changes described in the following paragraphs are not all completed in the embryonic period of antenatal life, some of them indeed are in progress late in the fœtal epoch, but they are placed in association for the sake of clearness and fulness.

THE BRANCHIAL GROOVES AND PHARYNGEAL POUCHES. — The structures derived from these parts are:

1. From the first, the salivary glands, the external auditory meatus, the tympanic cavity, and the Eustachian tube;
2. From the second and the neighbouring parts, the tonsils, the middle lobe of the thyroid gland, and the posterior third of the tongue;
3. From the third, the thymus gland and a parathyroid;
4. From the fourth, the lateral lobes of the thyroid gland, and another parathyroid; and
5. From the fifth, the little known post-branchial bodies.

THE BRANCHIAL ARCHES.—The *osseous and cartilaginous structures* derived from them are:

1. From the first, the maxillary process and its derivatives (superior maxilla, zygoma of temporal, malar, internal pterygoid process of sphenoid, and palate), and the mandibular process and its

derivatives (lower jaw, and Meckel's cartilage with the malleus and incus);

2. From the second, the stapes, the styloid process, the stylohyoid ligament (which may ossify), the lesser cornu of the hyoid bone, and probably part of the body of that bone;
3. From the third arch, the greater cornu and the rest of the body of the hyoid;
4. From the fourth, probably the thyroid cartilage of the larynx; and
5. From the fifth, possibly a part of the thyroid cartilage.

The *nerves* of the arches are:

1. Of the first, the second and third divisions of the fifth;
2. Of the second, the seventh and eighth;
3. Of the third, the ninth or glosso-pharyngeal;
4. Of the fourth, the superior laryngeal branch of the tenth nerve or vagus; and
5. Of the fifth, the inferior laryngeal branch of the vagus.

The *arteries* of the branchial arches, consisting of five[1] aortic arches on each side, arising from a ventral stem and joining a dorsal one, are transformed into the following permanent arteries:—

1. The first aortic arch disappears, unless the internal maxillary artery represents it, and the ventral stem becomes part of the external carotid, while the dorsal stem becomes part of the internal carotid;
2. The second aortic arch also degenerates, to be indicated possibly by the future lingual artery;
3. The third arch along with its dorsal stem and that of the second and first arches becomes the internal carotid artery;
4. The fourth arch on the right side becomes the first and second parts of the subclavian artery and its lower part disappears, while on the left side it forms the permanent aortic arch;
5. The fifth arch on the right side in great part disappears, while that of the left side remains as the ductus arteriosus.

THE CEREBRAL VESICLES.—Each of the five cerebral vesicles consists primarily of five parts,—a roof-plate, a floor-plate, an alar lamina or dorsal zone of the lateral wall on each side, a basal lamina or ventral zone of the lateral wall on each side, and a cavity. Each of these five parts may have a representative or representatives in later development.

1. *The Myelencephalon.*—From the myelencephalon, which, as a whole, becomes the medulla oblongata, the following are derived:—
    (*a*) From the roof-plate, the posterior velum.
    (*b*) From the floor-plate, the median raphe.
    (*c*) From the alar laminæ, the nuclei of the sensory roots of some of the cranial nerves, the nuclei of Goll and Burdach, and the olivary bodies.
    (*d*) From the basal laminæ, the nuclei of the motor roots of some of the cranial nerves, and the formatio reticularis.
    (*e*) From the cavity, the posterior part of the fourth ventricle.
2. *The Metencephalon*, as a whole, becomes the cerebellum and

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[1] Some embryologists maintain that there are six.

pons. Its connection with the mesencephalon constitutes the isthmus rhombencephali. Both these parts are represented by certain structures; therefore those arising from the isthmus are placed separately—

(*a*) From the roof-plate, part of the posterior velum and the vermis of the cerebellum.
(*b*) From the floor-plate, the median raphe (?).
(*c*) From the alar laminæ, the lobes of the cerebellum, the flocculi, the nuclei of the sensory roots of some of the cranial nerves, and the nuclei of the pons (?).
(*d*) From the basal laminæ, the nuclei of the motor roots of some of the cranial nerves and the formatio reticularis (?).
(*e*) From the cavity, part of the fourth ventricle.

2*a*. *The Isthmus Rhombencephali* gives origin, in all probability, to the following structures:—

(*a*) From the roof-plate, the anterior velum and the valve of Vieussens.
(*b*) From the floor-plate, the median raphe.
(*c*) From the alar laminæ, the superior peduncles of the cerebellum or brachia conjunctiva.
(*d*) From the basal laminæ, the posterior part of the crura cerebri and the posterior part of the tegmentum (?).
(*e*) From the cavity, part of the fourth ventricle.

3. *The Mesencephalon*, as a whole, gives rise to part of the crura cerebri and to the corpora quadrigemina, but it is not exactly known in what manner. The following is an incomplete and tentative arrangement:—

(*a*) From the roof-plate, some part not identified.
(*b*) From the floor-plate, the median raphe.
(*c*) From the alar laminæ, the corpora quadrigemina.
(*d*) From the basal laminæ, the nuclei of the third and fourth cranial nerves, the anterior part of the tegmentum, and the anterior part of the crura cerebri.
(*e*) From the cavity, the iter or aqueduct of Sylvius.

4. *The Diencephalon* or *Thalamencephalon*, which, as a whole, constitutes the optic thalami, the corpora albicantia, and the pineal body, gives rise in detail to the following parts:—

(*a*) From the roof-plate, the velum interpositum and the pineal gland or epiphysis.
(*b*) From the floor-plate, the tissue of the mid-ventral line.
(*c*) From the alar laminæ, the optic thalami, the pulvinares, and the external geniculate bodies.
(*d*) From the basal laminæ, the subthalamic region, the corpora albicantia (corpora mammillaria), and the tuber cinereum (part).
(*e*) From the cavity, part of the third ventricle.

5. *The Telencephalon*, which, as a whole, gives rise to the cerebral hemispheres, corpora striata, olfactory lobes, and infundibulum, is converted into the following detailed structures:—

(*a*) From the roof-plate, the anterior part of the velum interpositum (in the median part of the telencephalon) and the floor of the choroidal fissure (in the hemisphere part).

(*b*) From the floor-plate, the infundibulum and part of the pituitary body (hypophysis).

(*c*) From the alar laminæ, the lamina terminalis and optic evaginations (in the median part), and the pallium or mantle, the corpora striata, and the olfactory lobes (in the hemisphere part).

(*d*) From the basal laminæ, the anterior part of the subthalamic region and of the tuber cinereum.

(*e*) From the cavity, the anterior part of the third ventricle, the lateral ventricles, and the foramina of Monro.

CHAPTER VII

General Principles of the Pathology of the Embryo, or Teratology: (1) Physiological Factor—Nature and Illustrations; (2) Amniotic Factor—Nature, Mode of Action, and Illustrations; (3) Germinal Factor—Nature, Mode of Action, and Illustrations.

From the perusal of the preceding chapters the reader will have got some ideas of the chronology of embryonic life. No attempt has been made to supply him with all the facts and theories of Embryology; for these he must look in the proper place, the standard works on Embryology. In this volume it is *Embryology in disorder*, or Teratology, with which we have to deal, and to devote more than five chapters to *Embryology in order* would be to show a loss of all sense of proportion and a forgetfulness of the main purpose of the book. It would be as out of place as a full treatise on Physiology in a work on Pathology. At the same time the writer has given these chapters to the subject in order to emphasise the close connection between Embryology and Teratology, and to leave impressed on the mind of the reader the idea that his investigations into teratological problems must be preceded by a knowledge of the normal progress of development if they are to be in any degree fruitful. Let us now pass from this excursus on Embryology and return to the consideration of the general principles of Teratology begun in Chapter I.

In the first section of this Manual, that dealing with the Pathology of the Fœtus as distinct from that of the Embryo, I pointed out that the peculiarities of fœtal pathology could in large measure be explained by the influence of three factors,—the environmental, the placental, and the embryonic. In other words, I showed that the physiology of the fœtus, as exhibited in the special environment of fœtal life and in the placental economy, determined to a large extent the characteristic manifestations of fœtal diseases; and I indicated that such peculiarities as were not thus to be accounted for might be due to the effects of morbid conditions which had arisen in the embryonic period of antenatal life, and been transmitted into the fœtal. I hope now to show that it is reasonable to think that in a somewhat similar way the peculiarities of the pathological manifestations met with in the embryo may be determined by the special physiological conditions of the embryonic period of life and by the transmission into embryonic life of morbid states and tendencies acquired in the germinal epoch. In both cases I seek for the explanation of the peculiarities of the pathological phenomena in the peculiarities of the physiology of the period of life under consideration and in the transmission into that period of morbid states acquired in the preceding one. The pathology of each period of antenatal life is influenced by the physiology of that period; and it in its turn influences the pathology of the succeeding period.

The Physiological Factor in Embryonic Pathology.

The peculiarities of embryonic pathology depend in the first place upon the peculiarities of embryonic physiology, and embryonic physiology, as I have already said, is simply Embryology, Ontogeny, or Organogenesis. Embryonic life is concerned chiefly with the formation, elaboration, and specialisation of the materials which compose the new organism. This is the fundamental fact in the physiology of the embryo; the character of constructive activity pervades the whole of embryonic life and gives to it its peculiar quality or attribute. Where all the manifestations of life are of this formative kind, it must of necessity follow that the disturbance of these manifestations by morbid causes will lead to malformations, or, if the disturbance be great, to non-formations. Defects in the building of a house show themselves not in dry-rot but in architectural anomalies and errors of construction. The pathology of the embryo has to do not with diseases but with malformations.

Physiology underlies, pervades, and dominates pathology. To understand embryonic pathology, then, it is necessary constantly to keep in mind embryonic physiology. The more fully it is realised that embryonic physiology means normal formation, the more easy it becomes to concede that embryonic pathology must mean abnormal formation. There can, I think, be no doubt that the distinctive characters of embryonic physiology (Embryology) are the chief causes of the peculiarities of embryonic pathology (Teratology); in this way embryonic physiology is the most important factor in embryonic pathology. Of course it is not claimed that the embryo has no functions apart from organ-formation; some of its organs very early begin to perform functions and so become liable to diseases as distinguished from deformities; but the main trend of its activities is constructive in character. The physiology of the heart in embryonic life consists in part in the rhythmical contractions which drive the blood through the vessels both intra- and extra-embryonic; but it also consists in the gradual elaboration of a simple sinuous tube, at first made up of two cavities, through the intermediate stage of a double-chambered organ, into a four-chambered heart, in which, however, the foramen ovale remains for the rest of antenatal life as one of the indications of the structural changes through which the viscus has passed. The pathology of the heart in embryonic life mainly consists in an arrestment of this process of ontogenetic elaboration at one stage or another, and in the effects upon the rest of the organ which such a deviation from the normal produces. It may also, perhaps, in some cases, consist in a hastening of some part of the process, such as premature shutting off of the various chambers of the heart. Since, however, the heart is also capable of contracting in such a way as to propel the blood through the vessels, it follows that it has this function interfered with and a true disease produced. I have taken the heart as an illustration, for it shows clearly this combination of functional activity with structural elaboration and the consequent combination of characteristic fœtal with characteristic embryonic life; but the heart is an exception to the general rule in embryonic physiology. Most of the organs during the embryonic period are fully occupied with one form of vital activity—formation—and have not yet begun to functionate in the manner characteristic of fœtal or postnatal existence.

To take another instance, physiological activity in the region of the neck of the embryo consists in the formation of the branchial arches and clefts, and later in their reorganisation and utilisation in the construction of the cervical tissues, lower jaw, and inner and middle ear. Pathological embryonic activity in this same cervical region will take the form of disorderly development of these parts, and in the persistence of certain structures or grouping of structures which are normally quite transitory. Instances of such anomalies are found in cervical fistulæ and auricles; while among monstrosities thus formed may be mentioned hypoagnathus or defective development of the mandible and its associated malformations. In the posterior end of the embryo, physiological activity shuts off the uro-genital sinus from the anus, and again interposes a septum between the urethra and the vagina (in the female). Pathological activity reveals itself in an interference with this delimitation, and may cause a persistence of the cloaca or of the sinus uro-genitalis.

These, then, are instances of the influence which the physiological (embryological) factor has upon the pathological (teratological) manifestations of embryonic life. Let it be repeated that fœtal life has mostly to do with the growth of tissues and organs, and embryonic life with the differentiation of tissues and organs. Diseases are the characteristic morbid phenomena of fœtal life, and deformities of embryonic life. Teratology, in a word, is Embryology in disorder; there is defective Ontogeny; the vital dynamics of the antenatal formative processes is under the influence of morbid agencies. In a very special way, therefore, the physiological factor dominates the pathology of the embryo, giving to it some at least of its outstanding peculiarities.

The Amniotic Factor in Embryonic Pathology.

Just as disturbances in the physiology of the fœtus make their effect felt upon the pathology of the fœtus chiefly through the intermedium of one organ (the placenta), so probably disturbances in the physiology of the embryo modify the manifestations of pathology in the embryo through the agency of one structure (the amnion). Morbid causes in fœtal life chiefly act upon the fœtus through the placenta; so probably morbid causes in embryonic life act chiefly through the amnion. The placental economy comes in between the maternal and the fœtal organisms; so to some extent does the amniotic economy come in between the maternal and the embryonic organisms. The immediate environment of the embryo is amniotic; so it must be admitted is that of the fœtus; but in the latter the placenta has greatly increased in physiological value, while the amnion has diminished, and so from the point of view of functional activity the placenta is the most important part of the fœtal environment. There is then a placental factor in fœtal pathology, and an amniotic factor in embryonic pathology. Disturbances in function or diseases arise through the placenta, disturbances in construction through the amnion.

This view, at any rate, is a feasible one, although it cannot be claimed that it has been proved for the human embryo. In animals, *e.g.* the chick, it seems perfectly clear that the normal evolution of the embryo is very immediately dependent upon the normal evolution of the amniotic folds. The appearance of the cephalic, caudal, and lateral folds in the extra-embryonic somatopleure, their regular growth until the embryo is completely surrounded by them, their entire separation from the body of the embryo by the interposition of the liquor amnii, and the final closure of the amniotic sac, constitute a series of complicated processes, the normal performance of which is essential for the orderly formation of the new organism. It is to Teratology, and more especially to Comparative and Experimental Teratogeny, that science is indebted for the demonstration of this important fact. I doubt whether the rôle of the amnion in the normal formation of the chick could ever have been predicted from the examination of healthy embryological specimens alone. Dareste and other experimental teratologists have made numberless observations which seem to show that irregular development of the amnion is an almost constant factor in the artificial production of monstrosities in the chick. Apparently these morbid effects are due to the pressure brought to bear upon the embryo by the non-separation of the amniotic membrane from various regions of its body or limbs. This may be a transitory condition, and complete closure of the amniotic sac and separation of the amniotic membrane may occur later; but the removal of the pressure does not restore the *status quo ante,* the embryo goes on developing along the morbid lines into which it has been directed, and the pathological process continues although the immediate cause be no longer evident. A good example of this action of the amnion is found in the sympodial or sireniform fœtus. In its production there is defective development of the caudal fold of the amnion and consequent pressure on the posterior end of the embryo. This leads to rotation and partial fusion of the lower limbs and of the two halves of the pelvis; thereafter the development of the amnion may be completed, but the pathological process initiated remains, growth continues, and sympodia is found at the end of embryonic life. Possibly the earlier the pressure is removed the less complete will be the rotation and fusion of the lower limbs.

It may, however, be urged, and with no little force, that it by no means follows that the amnion plays the same part in human embryogenesis as it seems to do in that of the chick. This is perfectly true; and every effort must be made to avoid hasty generalisations regarding human embryology derived from observations in comparative embryology. If it were known, however, that the human amnion in its development arose in the same manner as the corresponding structure in the chick, there would be a strengthened presumption that its abnormal development would produce similar teratological results in the human subject and in the chick. Unfortunately this information is not available. As has been shown in Chapter III., it is precisely regarding the mode of development of the human amnion that embryology is without knowledge. In the earliest known human ovum the amnion is already present. Further, what is known of the later stages of its formation rather suggests a manner of development differing in essential details from that met with in the chick. Consequently it cannot be safe to conclude that the amnion in human embryogenesis plays a part similar to that which it does in avian embryogenesis either under normal or under abnormal circumstances.

On the other hand there is evidence of a certain kind in favour of the presence of an important amniotic factor in human teratogenesis. There have been many cases of malformation and monstrosity in which the amnion was adherent to the deformed part of the fœtus, or in which amniotic bands and threads coexisted with grave structural anomalies (*vide* Chapter XI.). I have met with several instances of this: one was a fœtus with exomphalus, facial fissures, cleft palate, diaphragmatic hernia, a stunted condition of the right arm, ocular anomalies, and a sacral spina bifida, and from the sacral sac a band passed to the membranes in the neighbourhood of the exomphalic sac; two others were fœtuses with exomphalos, facial fissures, and digital defects; another was a case of anencephalus and spina bifida; and another was an example of multiple malformations of the digits. I have also examined cases in which the membranes were adherent to the head or to other parts of the fœtus. All the large teratological collections may be expected to contain specimens illustrating such bands and adhesions. Further, in cases of oligohydramnion it has sometimes been found that the scantiness or absence of liquor amnii was accompanied by the presence of various fœtal malformations. It must be remembered, also, that the presence of amniotic bands is not necessary for the theory of the amniotic origin of human malformations. It is reasonable to expect that amniotic pressure without actual adhesion may in some instances be effective in teratogenesis. It is also quite conceivable that an adhesion may exist at an early period of development, and, having accomplished its pathological purpose, may then be absorbed or lost to view in the morbid process which it has set up.

Evidence, therefore, is not lacking to support the view that the amnion in the human subject as in the chick is an important factor in teratogenesis,—evidence drawn from the study of human monstrosities themselves and not from experiments in avian embryogenesis. At the same time it is quite possible that other parts of the environment of the embryo may also be effective factors in the production of deformities. The chorion, the umbilical vesicle, and perhaps the allantois may all exercise a distinct, although as yet unknown and undefined, influence upon the morbid manifestations of embryonic life.

In writing of the pathology of fœtal life and its investigation, I laid special stress upon the necessity of carefully examining the placenta as well as the fœtus in every case. Now, in reference to the inquiry into the problems of teratology or embryonic pathology, let me emphasise the importance of a thorough scrutiny of the fœtal membranes and of the routine examination, microscopic as well as macroscopic, of all abortion sacs and their contents thrown off in the early months of pregnancy. What are most wanted at present are careful descriptions of monstrous embryos from abortion sacs, observations upon teratological conditions while the organism is still in the embryonic period of antenatal life. These are essential for the further progress of a knowledge of human teratogenesis, and they are at the present time the desiderata of embryonic pathology. Microscopical human monstrosities are, as a matter of fact, almost unknown.

Whether or not the amnion be the important factor in teratogenesis, there can be no doubt that with the embryo just as with the fœtus it is the peculiarity of the intrauterine environment which so powerfully modifies the morbid developments of antenatal existence. This environmental factor in itself serves to explain nearly all the apparently so inexplicable phenomena of teratology and fœtal pathology. "Nearly all," for a very little thought will suffice to suggest several problems which neither the factor of embryonic physiology nor the rôle of the amnion serve to elucidate. This leads to the consideration of the third factor in embryonic pathology, which I have termed the germinal or pre-embryonic.

The Germinal Factor in Embryonic Pathology.

Just as there was found to be an embryonic factor in fœtal pathology (Manual, Section I., p. 185), so in embryonic pathology there are traces of the projection into it of the results of morbid causes acting at a yet earlier period. The reader may have noticed that I have made no reference to double monsters in what I have written regarding the teratological manifestations of embryonic life. Yet as every one knows, the united twins are very prominent and important teratological productions. The reason of my silence hitherto is that I believe that the double (or triple) nature of the organism is generally (if not always) decided before the period of the embryo is reached. Let me try to make clear what is meant by this statement, and to show the effect of the generalisation upon the study of the pathology of embryonic life.

When there are twins in the uterus certain conditions may be met with. In the first place, each twin may be separate having its own placenta and membranes, and each of these separate twins may be perfectly well formed and normal in every way. Again, one or other twin or both twins may exhibit malformations; one, for instance, may be acephalic (placental parasite) or anencephalic (as in a case reported by James Carmichael, *Trans. Edinb. Obst. Soc.*, iv. 408, 1878), or both may be affected with hare-lip and cleft palate (as in Underhill's observation, *Trans. Edinb. Obst. Soc.*, vi. 2, 1881). In the third place, the twins may be united together by a band but be in all other respects normally formed, or the union may be so intimate as necessarily to entail a considerable degree of deformity. In the fourth place, the joined twins may be deformed in other parts of their bodies than those concerned in the structural union; they may, for instance, exhibit spina bifida, imperforate rectum, talipes equinus, and the like.

These being some of the conditions that may be met with in twin pregnancies, I hold that they are not all developed in the embryonic epoch. One twin may become deformed in this period of antenatal life, both twins may have their organogenesis so interfered with that they show malformations, and possibly two embryonic areas may become so merged as to produce joined twins; these things may conceivably occur in the embryonic period. The fact, however, that there are two organisms in the uterus has, I feel sure, been determined before the appearance of the blastodermic layers and the commencement of the life of the embryo (as that has been defined). The double nature of the organism, but not necessarily its teratological character, has been fixed in the pre-embryonic stage of antenatal life. Given the presence of twins in the uterus, then one or other or both are subject to the same influences which by their action produce monstrosities in the single embryo and diseases in the single fœtus, and may in consequence become monstrous or diseased. I do not now refer to the teratological nature of twins as twins, that is a matter which will be dealt with later; but I emphasise the statement that both the organisms in the uterus in twinning must, in passing through the embryonic period of their existence, be subject to the same morbid influences as act upon the single embryo and produce in it teratological results.

In addition, however, to this view of the subject, it must be borne in mind that the fact that there are two organisms in the uterus complicates the process of development by introducing the possibility of the action of the one organism upon the other. It is a well-known fact that if one twin die in utero it may, through the continued growth of the living twin, become flattened and be converted into the *fœtus papyraceus* or *compressus*, so well known to obstetricians; and recent observations have gone to show that this flattening may occur at a very early period in intrauterine life (Loennberg, *Monatsch. f. Geburtsh. u. Gynäk.*, xvi. 25, 1902). It is also believed by some writers that one of the twins may not only influence the post-mortem fortunes of the other, but may even affect its normal growth and health. In the antenatal struggle for life and normal evolution, which is thus supposed to be set up in utero, it is conceived that the twin with greatest vitality and energy will gain an advantage over the other, will annex for his own benefit a larger area of the vascularised chorion than is his by right of equal division, will obtain a greater amount of nourishment, and will, in a phrase, become the predominant partner. As a result, the other twin will be less well nourished, will lag behind in its developmental processes, and may in the end be reduced to the subordinate position of becoming a pensioner upon his brother's bounty. A condition in which there were two organisms in the uterus, each equally parasitic upon the maternal system through the placenta, has then been replaced by a status in which one of the organisms is a maternal parasite, while the other is a parasite upon this parasite. In this way, therefore, twinning, a pre-embryonically determined condition, comes to play a part in embryonic pathology.

One need not, however, accept this explanation of the success of one twin and the failure of the other. There is another possibility. It may be necessary to look for the primary cause in germinal or pre-embryonic existence. That there are to be twins has been settled before embryonic life begins; that one of these is to be stronger and the other weaker while both are yet in the germinal stage may also have been decided. One of the twins, if this view be taken, may be so weak that its development cannot proceed beyond an early and most rudimentary stage; but through the circumstance of its twinship, and with the help of its co-twin, it is saved from certain early death, and enabled to live on in utero, sometimes without a heart, generally without any placenta or part of a placenta to call its own.

Of course it must never be forgotten that it is going beyond the bounds of strict accuracy to speak about such a thing as the struggle for life in utero and success or failure in this struggle; whether we regard the action of one twin on the other as maleficent or beneficent is not of so much importance as to bear in mind that we are applying figurative terms to the results of processes in which, of course, the idea of motives does not enter. The point upon which special stress is laid is that in embryonic pathology there are peculiarities, for the explanation of which it is necessary to look in the occurrences of the germinal period of antenatal life.

A still more cogent reason for believing in the existence of the germinal factor in embryonic pathology is supplied by the frequently observed heredity of some malformations. Sometimes it is found that such an anomaly as polydactyly, polymastia, perodactyly, cleft palate, etc., recurs in one generation after another; sometimes several members of the same family show the same structural anomaly; and occasionally a woman gives birth to several deformed children by one husband and to several healthy ones by a second consort. In all such cases it seems necessary to predicate the existence of morbid tendencies prior to the embryonic epoch.

It is not claimed that the appreciation of the presence of these three factors (physiological, amniotic, and germinal) will clear up all the problems of embryonic pathology. Alas! no. There is no such easy accomplishment of our task. It is believed, however, that it will throw some light upon teratological processes, enough light, perchance, to reveal that there are guiding principles and general laws at work where all appears chaotic, disordered. It is something to have realised that Teratology is Embryology in disorder; it is more to perceive that even this disorder is ruled by laws, is truly kept in order by them. After all, let us check any feeling of pride in the scientific achievements of these last years in the realm of Teratology by listening to the definition of a monstrosity framed by Aristotle[1] in the fourth century B.C.—

"The monstrosity is contrary to Nature, not contrary to Nature taken absolutely, but contrary to the most usual course of Nature. Nothing, in fact, can be produced contrary to that Nature, which is both eternal and essential."

Have we advanced at all in our conception of the real nature of teratological phenomena since the days of the great philosopher of Stagira, who "grâce à l'étonnante pénétration de son coup d'œil, a deviné une foule de vérités que les siècles postérieurs n'ont fait que confirmer, après une longue série d'observations"? But let us take heart; he also believed that there was order hidden behind the seeming disorder. With our gaze focussed upon the things that are near we see only the disorder, but with a wider view, taking in the whole horizon and rising therefrom to the zenith, we may catch a glimpse of the eternal purpose.

[1] Aristotle, *Περὶ ζώων γενεσέως*, lib. iv. ch. iii.

CHAPTER VIII

Teratogenesis or the Theories of the Causation of Monstrosities: Theories of the Past; General Survey; Theory of the Supernatural, with the Gods, or the Evil Spirits, or the Stars as Teratogenic Factors; Theory of the Natural, with Seminal and Menstrual Conditions and Hybridity as Teratogenic Factors.

In the preceding chapter I have given some account of what may be called the modern view of the nature of monstrosities, and have enumerated certain factors which, I believe, give to the pathological phenomena of embryonic life some at least of their distinctive characters. But it is now necessary to turn for a little while to the consideration of the theories regarding the nature and causes of teratological occurrences which were held in early times. Thereafter I shall refer to some more modern views, and so bring the reader back again to the embryological theory of teratogenesis, which has been already sketched in outline in Chapter VII. In dealing with the theories of the past I shall not encumber the text with many bibliographical references; these may be found by those who are desirous of consulting them in a series of articles on "Teratogenesis" which appeared in the *Transactions of the Edinburgh Obstetrical Society*, vol. xxi., 1896.

From the earliest times of which we possess any knowledge, attempts have been made to explain the occurrence of teratological phenomena. Many have been the theories; great has been the difference of opinion. Recently, however, real progress seems at length to have been made; and science now possesses a wider and more accurate knowledge of the causes which lead to the production of monstrosities and of the manner in which they act.

Some of the views held by the ancients regarding the cause of monstrous births have long since been abandoned or exist only among savage races of a low type; others are still accepted by the popular mind, but rejected by the scientific; and yet others have found a certain degree of justification in the results of the clinical and pathological investigations of the present age. In addition to the ideas handed down to us as a heritage from past times there are those which have been brought into being or confirmed in existence by modern scientific research. Experiment, that exact method so much vaunted in these times, has been brought into play, with results that have been regarded as of immense importance; a new science has, in a sense, been born, that of experimental teratogeny. With this attempt to solve the problems of Teratology by means of the artificial

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and experimental production of monstrosities I shall have to deal ere long; but it may be remarked in passing that the animals experimented upon have either been low in the Vertebrate series or have been among the Invertebrata. It follows, therefore, that we must not hastily ascribe to these experiments upon chicks, sea-urchins, and the like an overwhelming importance in the study of the monstrosities which occur in the human subject. Neither, however, can we afford to neglect the evidence regarding teratogenesis which they furnish.

In the meantime let us try to reconstruct from such materials and records as are available the teratogenetic theories of the past.

Theories of the Past.

I. THE SUPERNATURAL.

In the early ages of the world's history, dimly discernible now through the mists that have gathered over them, it was customary to ascribe all unusual phenomena of Nature—earthquakes, comets, solar halos or coronæ, eclipses, and the like—to supernatural causes. Abundant evidence of this is to be found in the literature and legends of the past, and in the customs and beliefs of savage or primitive peoples existing at the present time, but representing in such matters former times. Among the phenomena of Nature, justly regarded as unusual, a place could hardly be refused to malformations and monstrosities of the human fœtus or of the young of the lower animals; so it happens that in the earliest records of Teratology are to be found indications that such occurrences were regarded as due to supernatural agencies.

In different parts of the world, and in the same part but at different times, opinions differed as to the nature of the supernatural teratogenic cause and the meaning of the teratological phenomenon. When we read over these varied beliefs we are tempted to the conclusion that primitive man had a lively imagination, but a little thought is sufficient to make it likely that he is not to be accused of romancing and of inventing meaningless absurdities; he studied Nature and Life keenly no doubt, and read the meaning of their phenomena to the best of his ability with the little knowledge that he possessed. Various influences, geographical surroundings and the like, gave a colour to the beliefs of each particular race, and so helped to produce the diversity which we wonder at.

Some peoples ascribed monstrous births to the gods they worshipped; other races, who had divided their pantheon into good and evil deities, put the blame sometimes upon the former and sometimes upon the latter; whilst yet others connected teratological states with the positions and mode of combination of the stars and other heavenly bodies. Polytheism in some countries gave place to monotheism; yet the same ideas lived on, but were altered in their details to suit the newer conceptions of the supernatural. To the God of the Jew and the Christian, to the Satan of the Old Testament and the evil spirits of the New, and to the stars in the midnight sky, men still looked as the causes, direct or indirect, of the deformities with which an infant might come into the world.

The meaning, also, of the teratological phenomenon was variously conceived. The gods were amusing themselves, said some; they were exhibiting the extent of their creative powers, said others; they were angry with men, they were warning mankind, or they were chastising individuals or nations, were the views of yet others. From such beliefs by an easy transition came the idea that monstrosities were portents of events in the future, that they foretold sometimes good, but more commonly evil fortune. The Chaldeans read in the starry heavens the secrets of the future, and rapidly learned to transfer to the monstrous infant born under this or that astral combination the meaning of the stellar message; and so in ancient Babylonia the birth of a babe of doubtful sex meant an approaching calamity to the land, whilst the appearance of one with an imperforate anus proclaimed a famine! Similar astrological beliefs were in vogue in Europe in the Middle Ages; but they did not reign alone, for a transference of teratogenic powers had (it was thought) taken place from the deity to the devil, and to the malign influence of the tempter and his emissaries—the mediæval succubi and incubi—were ascribed monstrous and malformed births. Happy was the mother of a deformed infant when there was found a preponderating amount of evidence in favour of the stellar origin of her abnormal progeny; otherwise she might hardly escape a death at the stake, she and her "devil's brat."

Such were the various ways in which the supernatural was invoked to explain the origin of malformed fœtuses. Let us look, now, more in detail at the different phases of this ancient belief.

A. The Gods as Teratogenic Causes.

It is possible that in the earliest ages of the world's history monstrous infants were regarded as divine, and worshipped. They might be the gods themselves or their progeny, or they might simply be simulacra of the deity. This view may be called euhemeristic, and for the following reason. Euhemerus was an ancient historian of Sicily (he lived about 316 B.C.), who wrote a book (long since lost) in which he maintained (as the *New English Dictionary* tells us) that the deities of Hellenic mythology were deified men and women; and so euhemerism means "the method of mythological interpretation which regards myths as traditional accounts of real incidents in human history." On this euhemeristic hypothesis it is easy to account for the teratological appearances of many of the heathen gods and demigods. Of course, some of them are unlike the cases of monstrosity met with at the present time, but then it must be remembered that facts handed down by oral tradition from distant times and through the agency of men unacquainted with anatomical details, must inevitably be distorted. Doubtless the artificer of the idol was seldom, if ever, an eye-witness of the appearances of the deformed infant, and was consequently compelled to draw upon his imagination in order to eke out the exiguous data handed down to him to work with. Possibly, also, as Schatz has suggested in an interesting address (*Die griechischen Götter und die menschlichen Missgeburten,* Wiesbaden, 1901), each race would pick out those monstrosities which accorded most nearly with its particular notions of what its gods should be. The Greeks, for instance, in their deity-construction seem to have made no use of such wonder-exciting monstrosities as the acephalic placental parasites and the various types of united twins; and this fact may be due to the national taste which led to the selection of monstrosities that were not in themselves ugly or inartistic. Schatz goes on to point out that in the case of the cyclops fœtus there are two types, an ugly one and one which might in comparison be termed pretty; the Greeks took the pretty (!) one for the construction of the god Polyphemus; further, the nose which in the monstrous infant lies above the single eye was put in its proper (æsthetic) position below the eye. Figs. 18 and 19 will give an idea of the two types of cyclopia.

Perhaps, then, we may euhemerise the Siren into the sympodial fœtus (Fig. 20), the Centaur into the infant born with two pairs of lower limbs or into a hydrocephalic calf, the Gorgon head into an acormic placental parasite, Atlas into a case of occipital encephalocele, Janus into the diprosopous monstrosity, and Prometheus with his liver being torn by the vulture into an instance of fœtal exomphalos. At any rate the god Pthah of the Egyptians would seem clearly to have been an example of achondroplasia. So it may be that teratological specimens have served to supply the races of mankind with many of the deities which they have worshipped. The gods then after all did not create men, but men made the gods! Thus, in a novel sense, we may say "*sæpe visæ formæ Deorum.*"

To take up another line of thought and one that commended itself more to the ancients than did the hypothesis of Euhemerus: the gods were the creators of monstrous infants, and their purpose was amusement. Ζεὺς παίζει, Jupiter is playing, said Heraclitus; and Pliny (*Nat. Hist.*, lib. vii. c. 2) only slightly altered the idea when he wrote that "Nature creates monsters for the purpose of astonishing us and amusing herself,"[1] or as it has been quaintly rendered by his translator (P. Holland, *Translation of Pliny,* vol. i. p. 157, London, 1601), "see how Nature is disposed for the nones to devise full wittily in this and such like pastimes to play with mankind, thereby not onely to make her selfe merrie, but to set us a wondering at such strange miracles." Traces of this old belief are to be found at the present day in our use of the word "sport" in Botany, in the German "Spielart" and "Naturspiel," the French "jeu de la nature," and in the Latin "lusus naturæ," as synonyms of monstrosity. "Freak of nature" conveys a somewhat similar idea.

Soon, however, the notion of the sportive, pleasure-loving deities turning out monstrosities very much like children making mud-pies gave place to another and a graver conception. The gods were still the cause, and they were still friendly or at least not actively

[1] "Ludibria sibi, miracula nobis ingeniosa fecit natura."

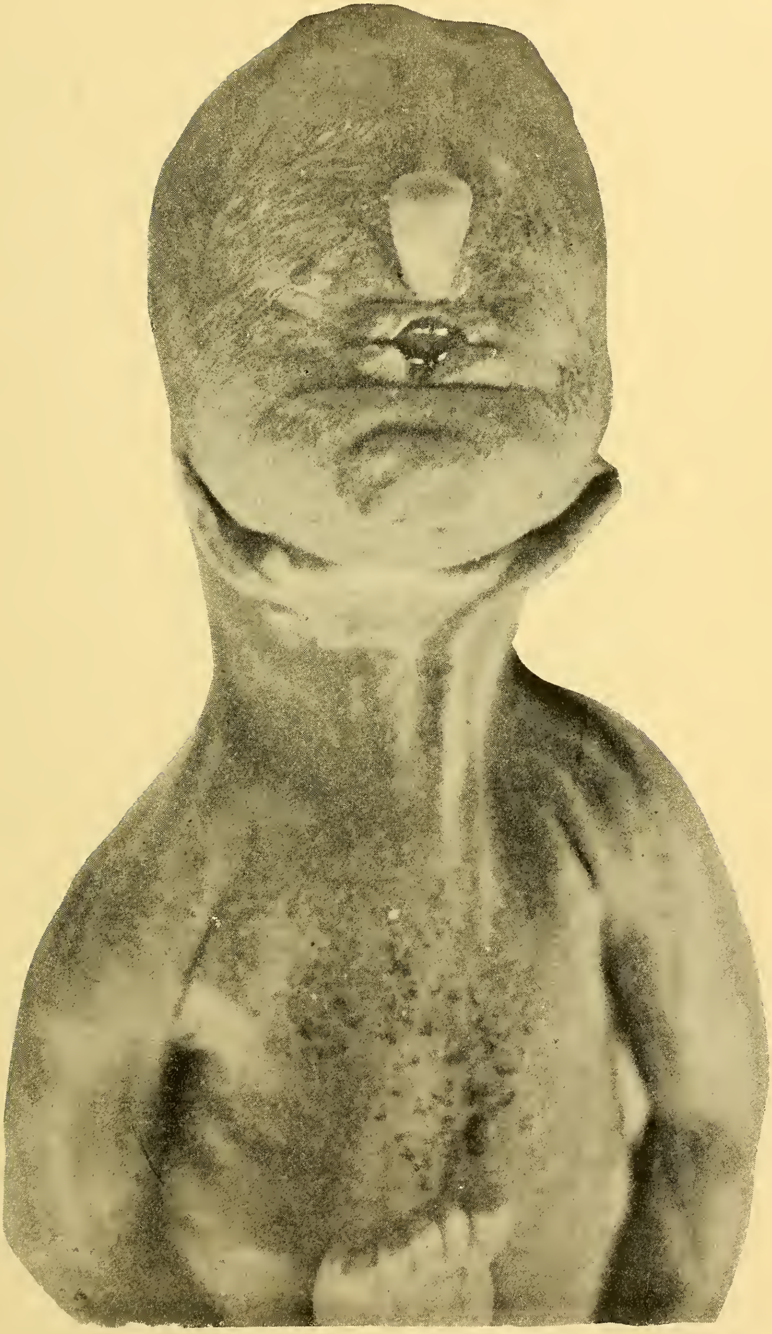

FIG. 18.—Head and upper part of trunk of Cyclops Fœtus with nasal proboscis, without mouth (astomus) and with ears displaced (synotus). Specimen No. 270.

unfriendly; but now their purpose was to warn, admonish, or threaten mankind. The belief in the monitory or minatory meaning of teratological occurrences took a firm hold on the minds of men, and the introduction of Christianity only meant the transference to the one God of the power and purpose that had been previously ascribed to the many deities of the Greek and Roman pantheon. It may be that the word *monster* itself is derived from *moneo*, I warn; but another origin has been suggested for it, to which reference will immediately be made. The birth of a deformed infant, then, was a Divine warning; it meant, further, that a deity must be propitiated, else some calamity would happen. From this belief to the destruction of the malformed infant is but a step, and thus doubtless arose one at least of the reasons why such monstrosities were, in Europe at any rate, almost invariably killed during the Early and Middle Ages. The Greeks of Sparta may have thrown their deformed infants into the abyss near Mount Taygetus in order to preserve or foster the physical perfection of the race; but in other countries the killing was sacrificial and propitiatory, and fortunate was the mother if she escaped her infant's fate. Julius Obsequens (*Prodigiorum Liber*, pp. 86, 103, Basileæ, 1552), for instance, states that in the year 120 B.C., "in foro Vessano androgynus natus in mare delatus est"; and again, in 92 B.C., "Androgynus Urbino natus, in mare deportatus." Lucan (*Pharsalia,* lib. i. verse 589), also, relates

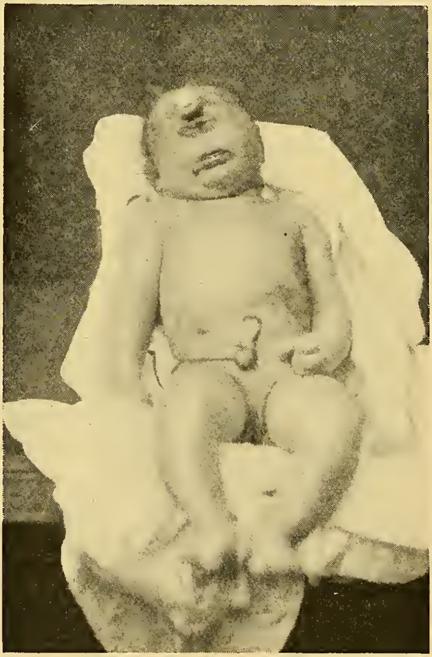

FIG. 19.—Cyclops Fœtus, with nasal proboscis, which occurred in the practice of Dr. J. W. Rodgers of Bristol (Nov. 13, 1891).

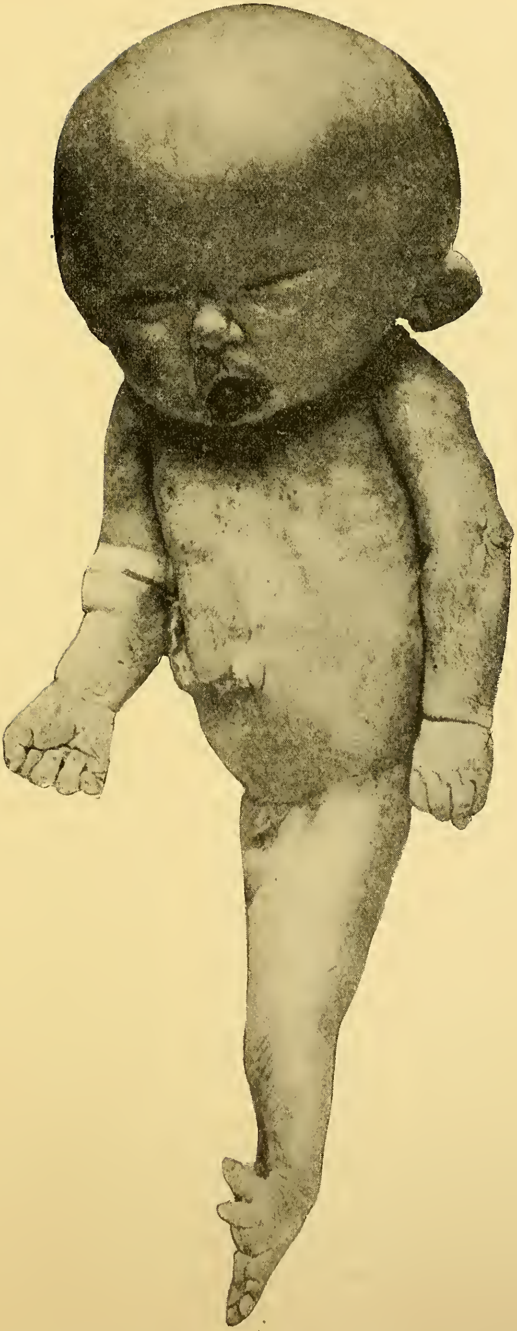

FIG. 20.—Sympodial or Siren Fœtus. Specimen No. 121.

how Arnus, the chief of the Etruscan diviners, ordered the slaughter and burning of all monstrous infants at the time of the overthrow of the Roman Republic.

Gradually it would appear that the idea of the deity as the cause of the monstrosity became lost in the consideration of the calamity which the malformed infant was supposed to predict, portend, or presage. The supposed cause of the phenomenon was lost sight of in the supposed effect. In this way it is believed that the word *monstrum* originated, namely, from *monstro,* I declare or show; and, as Cicero puts it (*De Divinatione,* lib. i. par. 42), "Monstra, Ostenta, Portenta, Prodigia appellantur, quoniam monstrant, ostendunt, portendunt, prædicant." Numerous instances might, in fact, be given of the pretended connection between monstrous births and national or personal calamities and misfortunes; the works of Lycosthenes (*Prodigiorum ac ostentorum chronicon, quæ præter naturæ ordinem, motum, et operationem, et in superioribus et his inferioribus mundi regionibus, ab exordio mundi usque ad hæc nostra tempora, acciderunt,* Basileæ, 1557), Obsequens (*op. cit.*), Boaistuau (*Histoires prodigieuses,* Paris, 1578), and others, are full of them. Perhaps, however, the most remarkable list of teratotogical occurrences with the events which they prognosticated or heralded is that which was literally unearthed by Assyriologists among the brick tablets of Asshurbanipal's library at Nineveh. I have elsewhere (*Teratologia,* i. 127, 1894) described at length this curious document with its cuneiform characters and its startling contents; startling indeed they are, for who could have expected to find among the ruins of the ancient civilisation of Babylonia a catalogue of monstrosities of the human infant, many of them quite capable of being identified by the present-day teratologist. The teratological tablet is reproduced in Fig. 21, and the reader who may be curious regarding the art of Teratoscopy as practised in Mesopotamia possibly 2000 years B.C. is referred to my article above mentioned. Sometimes the event predicted by the monstrous birth was of a fortunate nature, as when an infant with three legs (tripod) was born there would be great prosperity in the land, and when Cæsar's horse with feet showing digits served as an indication that the world would one day belong to his master (*Suetonius*). Notwithstanding some active opposition on the part of such writers as Licetus and Polydore Vergil, the idea that monstrous births predicted disaster held its ground till the close of the seventeenth century. Who shall say that in certain minds it is even now dead?

There is evidence to show that a malformed infant was sometimes regarded as a punishment of sins committed. In early French history we read that Robert II. (the Pious), who succeeded Hugues Capet, married near the close of the tenth century his cousin (in the fourth degree) Bertha, daughter of Conrad, King of Arles, and widow of Eudes I., Count of Blois. For this reason the royal pair were excommunicated by the Pope. The Queen gave birth to an infant having the head and neck of a goose (" une tête et un col d'oie "). Sismondi suggests that the monstrous infant was caused by the fright received

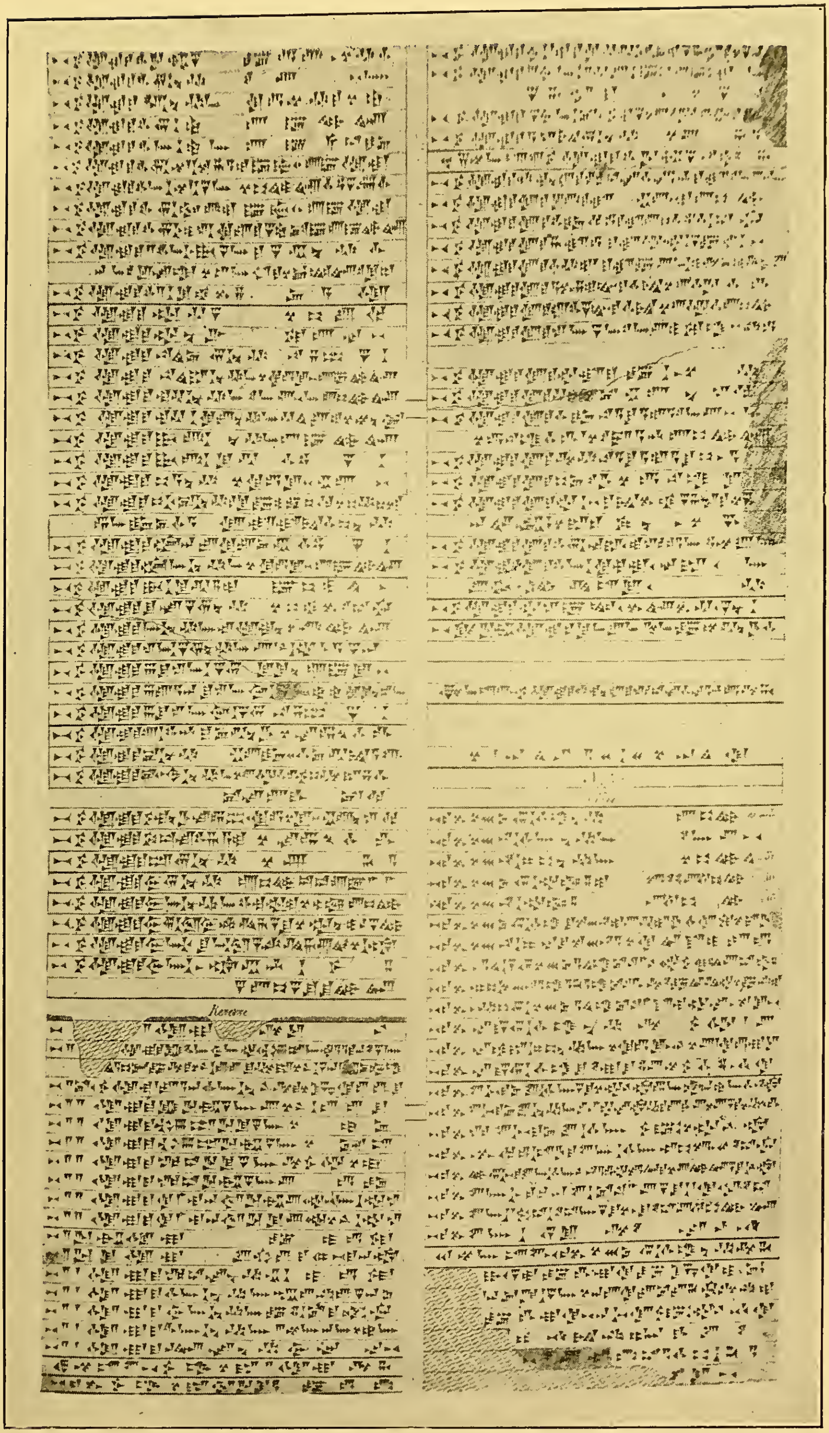

Fig. 21.—Chaldean Cuneiform Tablets with descriptive list of Monstrous Births. (*Vide Teratologia*, i. 127, 1894.)

by the Queen during her pregnancy from the papal excommunication; but Ségur (quoted by E. Martin in his *Histoire de monstres*, p. 78, 1880) states that it was a punishment from God ("un punition de Dieu"). This display of what we may call the vicarious teratogenic power of the Pope seems to have brought Robert the Pious to his knees; at any rate Bertha was repudiated in 1006, and the King married the haughty Constance, daughter of the Count of Toulouse.

Possibly the disciples of our Lord had some thought of the punitive nature of congenital malformations when they put the question concerning the man born blind: "Master, who did sin, this man, or his parents, that he was born blind?" The reply probably gave rise to the view that monstrous births were for the purpose of revealing the glory of God. Paré, in his treatise on monsters, enumerates thirteen causes of such productions, of which the first is to proclaim the glory of God; to quote his translator (T. Johnson, lib. xxv. c. 1, p. 585, London, 1678): "There are reckoned up many causes of Monsters, the first whereof is the glory of God, that His immense power may be manifest to those which are ignorant of it, by the sending of those things which happen contrary to Nature." Expression was again given to this view in the discussions which took place towards the close of the seventeenth century on the pre-existence of germs. If normal germs pre-exist, why not also monstrous ones? This, however, Swammerdam and Malebranche would not admit, because that would be to confess that monstrous infants were the immediate work of the Creator. Régis, in his *Système de philosophie* (III., lib. viii. pt. 1, c. ix.), accepted this consequence, and explained that whilst normal beings showed forth the infinite wisdom of the Creator, monstrosities demonstrated His infinite power. Obviously this question does not stand alone, but forms one of a group (which contains the relation of the Creator to human disease and sin and disaster); its discussion would obviously be out of place here.

B. Evil Spirits as Teratogenic Causes.

It was inevitable that a belief in the teratogenic power of the deity should be followed sooner or later by the idea that this power was specially the possession of an evil or malignant spirit. Indications of this belief are to be found everywhere, and even at the present time the notion gets whispered about even if it be not openly stated. The history of the effects of this notion is full of sad, revolting, repulsive, and almost incredible incidents, and no good purpose can be served by lingering over it. Reference, however, may be made in passing to a piece of evidence which shows that the belief in the diabolical origin of monstrosities prevailed in Northern as well as in Middle and Southern Europe. Du Chaillu, in his work on the Vikings (*The Viking Age*, ii. 40), gives the following extract from an ancient legal enactment of the Norsemen: "Every child which is born into this world shall be reared, baptized, and carried to the church; except that only which is born so deformed that the mother cannot give strength to it. . . . It shall be carried to a beach and buried where neither men nor cattle go; that is, the beach of the evil one." The exposure of the deformed infant was, however, one of the lesser evils associated with this theory of the production of monstrosities; but as I have said it is unprofitable to inquire further into this darkest fancy of the Dark Ages.

C. The Stars and Moon as Teratogenic Causes.

The position, movements, and combinations of the heavenly bodies have entered largely into the formation of the opinions and beliefs of ancient races concerning the origin of terrestrial phenomena. The Chaldeans were, as is well known, past-masters in the art of divination from all kinds of phenomena, stellar or terrestrial. That they connected together teratological and astrological occurrences is also beyond doubt. Lenormant, in his work on Chaldean divination (*La Divination et la science des présages chez les Chaldéens*, p. 103, Paris, 1875), explains in a very reasonable way how this belief grew. The passage may be rendered as follows: "The development that their astrology had given to genethlialogy or the art of horoscopes of births, had led them early to attribute great importance to all the teratological facts which were there produced. They claimed that an experience of 470,000 years of observations, all concordant, fully justified their system, and that in nothing was the influence of the stars marked in a more indubitable manner than in the fatal law which determined the destiny of each individual, according to the state of the sky at the moment when he came into the world. Cicero, by the very terms which he uses to refute the Chaldeans, shows that the result of these ideas was to consider all infirmities and monstrosities that new-born infants exhibited as the inevitable and irremediable consequence of the action of these astral positions. This being granted, the observation of similar monstrosities gave, as it were, a reflection of the state of the sky, on which depended all terrestrial things; consequently one might read the future in them with as much certainty as in the stars themselves."

Astrology and the casting of nativities survived by many centuries the fall of the Babylonian empire and the special Chaldean genethlialogy; indeed, the notion of stellar influence upon the fœtus lives still in the expression "born under a lucky star," and Zadkiel's Almanac is a solid fact. In the popular mind there was all along a sort of intermittent and sneaking regard for such beliefs, although the learned might slight "the art of those foolish Astrologers, and Genethliacall Ephemerists, that use to pry into the horoscope of Nativities"[1] and write of the "Genethliack and Horoscopal fool."

Ptolemæus Claudius, an Alexandrian astrologer of the second century, not only stated the astral conditions under which terata were born, but also mentioned the nature of the malformation to be expected (*Tetrabiblon*, lib. iii. c. viii.; quoted by Taruffi, *Storia della Teratologia*, iv. 18, 1886). The position of Venus or of the moon at the moment of conception had, according to the astrological doctrine, a potent effect in determining whether the infant was to be normal or deformed. About the year 1200, a cow gave birth to a deformed calf, said to be half human, and the shepherd in charge thereof, being suspected of an unnatural crime, was condemned to be burned alive. Fortunately for him, however, Albertus Magnus (1193–1280), that most voluminous writer upon so vast a number of different subjects, came forward with the explanation that the teratological phenomenon was due to a certain constellation; so the shepherd's life was saved. In *De animalibus*, one of the works of Albertus, it is accordingly stated that a monstrosity may be due either to a fault in the "material" or to celestial influence; when certain heavenly bodies are found in certain places in the sky a man cannot be generated, and so a child is born with the head of a bull or a lamb. Thomas Aquinas (1225–1274), "the Angelic Doctor," a disciple of Albertus, accepted these theories, and even expounded them to some extent. Cardanus, a prolific writer of the sixteenth century (1501–1576), notable for the extraordinary mixture of sagacity and obtuseness in his works, moulded his beliefs upon those of Ptolemy already referred to; he even supplied his readers with the representation of the constellation under which a double monster was born. Septalius (*Libr. de Nævis*, Mediolani, 1606) looked to the stars for the explanation of moles and nævi seen on the fœtus; and even T. Bartholin (*De cometâ consilium medicum, monstrorum nuper in Dania natorum historia*, Copenhagen, 1665) believed in the potency of stellar influences upon the unborn infant. In a work entitled *Grande Encyclopédie Universelle*, by Henricus Asteldius, published about the beginning of the seventeenth century, it is stated that a Danish astronomer, who was also a medical man, had discovered the origin of monstrosities. He ascribed them to comets, and regarded them as tumours scattered throughout the firmament, which when they were precipitated upon the earth, took on there all kinds of unusual and extraordinary forms (E. Martin, *op. cit.*). In the work by Aldrovandus (*De monstrorum historia*, p. 391, Bononiæ, 1642), edited by Ambrosinus, credence is given to the foregoing beliefs; at any rate the views are stated, and their adherents named. Ambrose Paré, however, is openly sceptical, and says (to quote again his English translator, Th. Johnson): "Yet astrologers (lest there should seem to be anything which they are ignorant of) refer the causes of these (*i.e.* monsters) to certain constellations and aspects of the planets and stars." Licetus (*De monstris*, lib. i. cap. vi., Patavii, 1668) altogether omitted the stars from his list of teratological causes, and so the theory died out, at least among the scientific and so to say the official teratologists.

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[1] Howell, *Dodona's Grove*, p. 191, 1640.

Among the heavenly bodies the moon has always held a high place in so far as her effect upon mundane affairs was concerned, and a trace of a belief in her teratogenic powers is preserved in the word "moon-calf." This word has three meanings given to it in most English dictionaries. In Webster's *Unabridged* (Goodrich and Porter), for instance, it is defined as (1) a monster; false conception; (2) a mole, or mass of fleshy matter generated in the uterus; and (3) a dolt; a stupid fellow. Ogilvie, in the *Imperial Dictionary* (New Edit., iii., 1882), gives the same three meanings, and adds that it is comparable to the German "Mond-Kalb," a person or conception influenced by the moon. In Foster's *Illustrated Medical Dictionary* (iv. p. 2337), its German equivalents are stated to be "Mondkalb" or "Mohnkalb," and it is defined as (1) a fœtal monstrosity, and (2) the translation of an old term for a fleshy mole. J. O. Halliwell, in his *Dictionary of Archaic and Provincial Words* (ii. p. 560, London, 1847), quotes Cotgrave's definition, "a moon-calfe, a hard swelling or shapeless peece of flesh in the wombe, which makes women beleeve they are with child when they are not," and goes on to state that the term was often applied to a monster or a fool, and that in Somerset a crying child is so called. As with so many other words, its earliest use in any of these three meanings is not known. Some authors refer back to Pliny, but, of course, the word used by him was mola. In the *Natural History* (lib. vii. cap. 15) it is said, "solum autem animal menstruale mulier est: inde unius utero, quas appellarunt molas. Ea est caro informis, inanima, ferri ictum et aciem respuens"; and again in lib. x. cap. 64 we read, "Molas, de quibus ante diximus, gigni putant, ubi mulier non ex mare, verum ex semetipsa tantum conceperit." Now, in Holland's translation of Pliny's works (1601), the word mooncalf appears as the equivalent of "mola": "of all living creatures, a woman hath a flux of bloud every moneth; and hereupon it is that in her wombe only there are found a false conception called mola, *i.* a moonecalfe, that is to say, a lumpe of flesh without shape, without life, and so hard withall, that uneth a knife will enter and pierce it either with edge or point," "as for false conceptions or moonecalves (whereof we spake before) some thinke they are engendred of the woman's seed only; namely when she is not conceived by a man but by herselfe." It is quite evident, therefore, that in the beginning of the seventeenth century the word "mooncalf" was regarded as a synonym of uterine mole; how much earlier I cannot say. In this sense it may be taken that the term "calf" meant not the young of the cow, but a swelling or lump (as in "calf" of the leg). Mooncalf might then be freely rendered "menstrual lump." In Viardel's *Accouchemens* (Paris, 1671) the word "mole" is used to signify a round mass engendered in the uterus; but it is very interesting to find in the German translation (Franckfurt, 1676) the term *Monkalb* or *Mutterkalb* used constantly as its equivalent. At the same time it is not clear that the term "Mon" meant the "moon" in this combination; perhaps rather it was allied to "Mönch," a gelding, and the Latin "mancus," defective, in reference to Pliny's idea that the woman who conceived the mass did so without impregnation.

It is not certain, then, that in this meaning the word mooncalf suggested a belief in lunar influence; but as a synonym of monstrosity it truly seems to have done so. This becomes apparent from several passages in Shakespeare's *Tempest.* In this play Caliban, the son of the "foul witch, Sycorax," is on several occasions called "a mooncalf," for example, "the siege of this mooncalf," and "the dead mooncalf's gaberdine," Act ii. sc. 2. He is described as "a freckled whelp, hag-born—not honour'd with a human shape," "half a fish, half a monster."

> "This misshapen knave,
> His mother was a witch, and one so strong
> That could control the moon, make flows and ebbs,
> And deal in her command, without her power."

Whether Shakespeare in this passage hinted at a connection between the witch-mother's control of the moon and her mooncalf son or is merely playing upon words is not clear, but the latter hypothesis is the more probable, for elsewhere in the *Tempest* the diabolical origin of Caliban is referred to. In its meaning of monster we may take it that mooncalf is derived from "moon" and "calf," the latter word signifying in Middle English, Anglo-Saxon, German, etc., the young of the cow or other animal, and being related to the Greek βρέφος (embryo), and to the Sanskrit *garbha* (fœtus or embryo); while "moon" may refer to this belief in the lunar influence on the unborn fœtus. So mooncalf may be defined as an embryo or fœtus become monstrous under the influence of the moon.

Such were the theories of the supernatural which our ancestors used to explain the occurrence of teratological phenomena, and while they may bring a smile to the face of the modern scientist, it must not be forgotten that their existence was a very real thing to the people of the Middle Ages, and that even at the present day traces of these early superstitions are to be found not only amongst savage races, but also in our own land and in the popular mind.

II. THE NATURAL.

It must not be supposed that the only teratogenic theories in vogue in past times were those which recognised supernatural agencies. As a matter of fact the early Greek philosophers looked for purely physical causes of monstrosities, and these they found in disturbances of the natural phenomena of reproduction. At the same time it must be borne in mind that the notions regarding generation which prevailed in the early Greek age, although vastly more correct than many of the fancies of the Middle Ages, were yet in certain points defective and even erroneous. Consequently the teratogenic theories founded upon them could not be free from mistakes. Such as they were, however, they held their ground for something like two thousand years, and even now their influence is to be felt in many of the doctrines of the day.

In order to understand these theories it is necessary to remember the views concerning reproduction which were held by the early Greek writers; these may be indicated in a few words. Since the invention of the microscope was still in the distant future, nothing was known of the existence of human ova and spermatozoa. The evident facts of the generative process were the seminal discharge in the male and the menses in the female. Some writers regarded the semen as the sole, or at least the principal, factor in reproduction;

according to them the woman was nothing save a temporary abode for the fœtus. Others were of opinion that the menses supplied the material for generation, and that the male semen was of comparatively little importance. Others, again, saw that both semen and menses were essential factors; and in words which have been ascribed to Aristotle, "The blood of the menses is the marble, the semen is the sculptor, and the fœtus is the statue." Somewhat similar views prevailed amongst the Romans. Pliny, for instance, in speaking of the menses says—I use the words of Holland's translation:—"In very deed it" (*i.e.* the menses) "is the materiall substance of generation: and the man's seed serveth instead of a runnet to gather it round into a curd; which afterwards in processe of time quickeneth and groweth to the forme of a bodie."

The menstrual blood seems sometimes to have been called the female semen, and the sex of the fœtus was supposed to be due to the greater strength of one of the two seeds. Another notion was that boys were generated in the right testicle and girls in the left; and yet another was that when the semen was deposited in the left side of the uterus a female embryo resulted, when in the right side a male.

Mention, also, must here be made of another belief concerning generation which had its origin far back in the history of the world, and in illustration of which many examples may be found in Greek and Roman mythology. I refer to the supposed fertility of animals of different kinds with one another, and even with man. Aristotle, even, believed in this view to a certain but small extent, and later authors accepted the theory in its widest sense, and with its most ludicrous developments.

The theories of the Greeks passed in process of time to the Romans. During the Dark Ages in Europe they were cherished by the physicians of Arabia, and so in process of time they came to be the views of the nations of Western Europe, when the revival of learning put an end to the epoch of intellectual barrenness. In many ways, however, the original lucidity of the classic theories was obscured during the long period which elapsed between the times of Hippocrates and Aristotle, and those of Paré and Licetus; and metaphysical notions abounded in the writings of the Middle Ages, greatly to the detriment of the purely physical notions of the Greeks.

The teratogenic theories of the past which looked for physical causes of monstrosities were based upon the study of the phenomena of generation as these were then understood; they were, in fact, deductions from them. Further, the various phases of the ideas concerning reproduction were all reproduced in the theories of the causes of teratological productions. Those writers, for instance, who regarded the male semen as the sole, or at any rate as the chief factor in generation, ascribed teratogenic properties to alterations in its quantity or quality. Others, considering the menstrual discharge as of prime importance in reproduction, looked to it as the cause of monstrous births. These two primary theories did not, however, long exist separate, for it soon came to be recognised that both parents might supply teratogenic factors; thus a sort of coalition hypothesis, in which now the seminal and again the menstrual element would predominate, came into being and long persisted,—persists in a certain sense still.

Alongside of these theories was constantly to be found that other which regarded teratological productions as the result of intercourse between animals of different kinds and between man and the brutes. This, also, as will be at once seen, was the direct outcome of the old notion of fertility between different genera.

A. Seminal and Menstrual Causes.

The theory that monstrous infants are the result of *unusual conditions of the paternal element in generation—the male semen*—is a very old one; it seems first to have been expressed by Empedocles of Agrigentum, in Sicily, a physicist living between the years 495 and 435 B.C. He has been called the "father of the evolution idea" (Osborn, *From the Greeks to Darwin*, p. 37, 1894), and seems to have had some knowledge of embryology and teratology. Empedocles, like Lucretius some four centuries later, recognised what may be called a teratological stage in the world's history when animals appeared, spontaneously generated, as incomplete individuals—"heads without necks, arms without shoulders, eyes without their sockets"—and when through the fortuitous union of these parts with one another all sorts of monstrous forms came into being, soon, however, to become extinct through the absence of reproductive powers. But it is rather with the views that this philosopher advanced to explain the origin of monstrosities, after Nature had succeeded in producing normal permanent animal types, that we have here to do. As Plutarch (*De placit. philos.*, lib. v. cap. 8) relates, Empedocles thought that monsters happened either from abundance or from defect of the semen, from slowness of movement, from division of it into several parts, or from aberration of the movement. Although five states are here enumerated, only three ideas really exist, these being the notions of excess, of defect, and of alteration of the semen. Curiously enough, these are precisely the ideas which underlie recent views, not, indeed, of the causation of teratological products, but of their classification. For the primary division of monstrosities into *monstra per excessum*, *monstra per defectum*, and *monstra per fabricam alienam*, which Förster employed, or into *monstra deficientia*, *monstra abundantia*, and *monstra sensu strictiore deformia*, as Otto recommended, cannot yet be said to have been improved upon. So in a certain sense it may be said that the views advanced so long ago by the Sicilian physicist live still; and there can be no doubt that they were widely accepted by Greek, Roman, and mediæval authors.

The teratogenic theories of Democritus of Abdera, another physicist of the same age as Empedocles, did not take a very firm hold upon the philosophic mind. As we are told by Albertus Magnus (*De animalibus*, lib. xviii. c. 6), Democritus thought that double monsters were generated when the semen belonging to one or to two species was introduced into the uterus repeatedly at intervals; to begin with, the first semen reached the womb and sufficed to form the new being; soon thereafter the second semen arrived, mixed with the first, and began to operate in its turn; and so the members came to be duplicated. The abuse of coitus was thus made out to be a teratogenic factor.

Neither Empedocles nor Democritus ascribed to the female any formative power in the matter of generation; Aristotle, on the other hand, did so; and, in consequence of this, his theory of teratogenesis included faults in the female element in reproduction as well as in the semen. The Aristotelian hypothesis, therefore, was one which recognised a dual cause, and as such it will fall to be discussed immediately; in the meantime it may be said that through its weighty authority the case of the theories which looked for solely a seminal or solely a menstrual teratogenic factor was greatly weakened. Nevertheless Galen, living in the second century of the Christian era, seems to have believed in a purely seminal theory, for he thought that hermaphrodites were due to the entrance into the uterus of spermatic fluid from both the testicles.

The Arabian physicians during the Dark Ages in Europe served to perpetuate the doctrines of the past, and prominently those of Aristotle; but Avicenna, like Galen, sought for an explanation of the origin of hermaphrodites along the lines of the older theories, for he believed that whilst semen deposited in the left side of the uterus resulted in the birth of a girl, and in the right side in that of a boy, the male element when placed in the middle of the cavity gave rise to the procreation of a hermaphrodite.

In Europe in the thirteenth and fourteenth centuries certain contributions were made to the study of the causes of monstrosities; but the question was greatly complicated by the introduction of the terms "materia" or "material" instead of semen, and by the supposition that this materia had a formative virtue or faculty. In this way confusion was the result, for "materia" came to be applied to the menses as well as the semen, and the "formative faculty" was an idea which encouraged all sorts of profitless theorisings. To some of these hypotheses allusion will be made immediately when the causation of monstrosities through faults in both male and female elements in generation is under consideration. Here it may simply be said that the theory of Empedocles never again came to be accepted fully, although the discovery by Leuwenhœk (in 1677) of spermatic animalcules in the semen gave a temporary support to the notion that after all the male element might be the chief, if not the sole teratogenic factor. With the discussion of the influence of the spermatozoa in producing monstrosities we have not at present to do; that is a matter to be considered along with the theories of the present, not with those of the past.

The idea that *the menses* play an important part in the generation of monsters seems largely to have been the result of the Hebrew legislation regarding coitus during or immediately after the flow. In a non-canonical book (Esdras, Book iv. c. 5, verse 8), the following statement occurs:—"Menstruous women shall bring forth monsters" (*mulieres menstruatæ parient monstra*); and in the Talmud the infant conceived during the period of impurity was regarded as certain to be an epileptic, a cretin, a drunkard, or insane. At the same time indications of a similar belief are to be found in the records of classic mythology, for it is said of Vulcan, who was so deformed at his birth that his mother in disgust threw him into the sea, that he was begotten by Jupiter when Juno was menstruating. Witkowski (*Histoire des Accouchements*, p. 335, Paris, 1887) refers also to this belief, which he regards as a very common one, and quotes the following lines in which it is embodied in verse:—

"Femmes qui désirez de la progéniture,
Durant le cours des mois respectez la nature;
Le fils de Jupiter, Vulcain, ainsi concu,
Vint au monde impotent, cul-de-jatte et bossu."

Aristotle and his followers did not admit the pre-eminence of the menses in teratogenesis; the menstrual blood or materia was only one factor in normal generation, and therefore also in abnormal generation. Nevertheless there were some who regarded the menstrual blood as of greater importance than the semen in the causation of monstrosities; thus Henricus of Saxony (*De secretis mulierum*, c. 6, 1478), a pupil of Albertus Magnus, regarded teratological phenomena as due to deficiency or excess of the materia or menses. Paré (*op. cit.*), also, amongst the numerous causes of monsters, places intercourse between parents at such times as they ought to forbear by the command of God and the Church. Licetus, writing in 1616, mentions the menstrual flow at the time of conception as the seventh cause of the origin of shapeless monstrosities, and founds his belief on the passage in Esdras already referred to, and on a quotation from Solinus.

When it is borne in mind that Pliny and many of the writers of the Middle Ages attributed to menstrual blood the most maleficent powers as regards vegetables, metals, glass, trees, and even animals, it is not to be wondered at that numbers of authors found in it one at least of the causes of deformed births. Towards the close of the seventeenth century, however, discoveries were made which revealed the hollowness of such beliefs; and it was from the investigations of Harvey and de Graaf, and from the light which they threw upon the true nature of the female factor in reproduction, that the menstrual theory of teratogenesis received its deathblow. We know now that anomalies in the female factor are frequently causes of monstrosities, but that factor is no longer the menstrual blood but the ovum.

B. SEMINAL-MENSTRUAL CAUSES.

The theory which regarded *alterations in both the male and female elements in generation* as the cause of monstrous forms may rightly be called the Aristotelian. Aristotle (384 to 322 B.C.), by means of his great intellect and strictly scientific methods of research by experiment and induction, placed all the workers who followed him in the position of debtors. Even in the subject of teratology his views were far in advance of his time. His definition of a monstrosity (*De generatione animalium*, lib. iv. c. 3 and 4) has already been stated (p. 80); it revealed an extraordinary degree of critical insight. Aristotle, also, refuted the opinion of Democritus concerning the origin of monstrosities; neither did he adhere to the theory of Empedocles, for he believed in the conjoint action of perverted states of both sperm and germ. He recognised the teratogenic power of faults in the materia which exists in the menstrual blood, and pointed out the more frequent occurrence of terata in the animals that produce many young ones. He was truly the founder of both human and comparative teratology, and as regards the latter subject his knowledge of the embryonic origin of double monsters in the hen's egg was really wonderful. Had he known that man also originates in an ovum, it is more than probable that he would have applied the facts of teratogenesis in the chick to human teratology, and so have discovered in the fourth century B.C. what has been reserved for the savants of the nineteenth century A.D.

The doctrines of Aristotle were handed down by succeeding writers, Roman and Arabian, to the times of the Middle Ages in Europe, when Albertus Magnus, the Dominican monk (1193 to 1280 A.D.), accepted, but with modifications, the views of the Greeks concerning the production of monstrosities. The modifications were most unfortunate, and were destined greatly to obscure the original theories. Thus, Albertus admitted the teratogenic powers of the semen, but he used the word *materia* as a synonym; those who followed him lost sight of the real meaning of the term, and thus great confusion was introduced. Again, Albertus ascribed to the stars the same powers in the production of monstrosities as he gave to the materia, and so lent his sanction to the supernatural notions of his time. He also believed with Aristotle that terata were less frequent in uniparous than in pluriparous animals. His disciple, Henricus of Saxony, held views to which reference has been already made. He seems to have regarded the materia as the menses, and he thought that all the causes of monstrosities might be reduced to two: disobedience of the materia, and its insufficiency. He introduced, also, such secondary causes as faults in the uterus preventing the retention of the semen, and the position of the body during coitus.

Thomas Aquinas, another Dominican of about the same period (1225 to 1274 A.D.), introduced the idea of a formative power or faculty which acted upon the semen; and, like Albertus Magnus, he ascribed teratogenic properties to the heavenly bodies. With him indisposition of the materia was the immediate, and the effect of the stars the remote factor in teratology. Pietro di Argelata added the notion of a formative power or faculty to the doctrine of the Greeks, for in writing concerning supernumerary and large and small digits, he admitted that they were caused by excess or defect of the materia, but only if these were combined with a strong or a weak formative power. The last-named factor was the more important; indeed, with only a small amount of materia, a large part might be produced if the formative faculty were sufficiently great. Possibly in such a case the formative power made the materia more obedient to movement and more capable of extension.

In the early years of the sixteenth century ample evidence was forthcoming in the writings of the time to show how confused the original Greek theories had become. Bonacioli (*Enneas muliebris*, c. ix.), an author of this age, seems to have returned to the views of Empedocles with regard to the formation of fœtuses with supernumerary parts, hermaphrodites, and monstrosities showing defects; he also complicated matters by referring to a materia supplied by the woman as well as by the man. About the middle of this century Savonarola (*Practica major*, tr. vi. c. xxi. f. 269, Venetiis, 1559) wrote at some length on the generation of moles from the semen and menses, reproducing largely the opinions of Avicenna; he stated that some women, from impurity of the blood, gave birth not only to a true fœtus, but also to a piece of flesh resembling an animal, *e.g.*, a toad, falcon, lizard, etc.; this was due to an error in the second semen, and this error was the result of stellar influence. Varchi (*Lezioni sopra la generazione dei mostri*, p. 101, Firenze, 1560), whilst he believed that the two principal causes of monstrosities were faults (qualitative and quantitative) in the male semen and in the menses of the woman, also recognised others, such as the state of the uterus and the secundines, the imagination, and the effect of the heavenly bodies. The last-named cause was introduced so as not to contradict the theologians.

Towards the close of the sixteenth and beginning of the seventeenth century the tendency, already seen in Varchi's writings, towards a multiplication of the causes of monstrosities became very evident. Paré, for instance, enumerated eleven different teratogenic factors, and Licetus gave even a larger number for selection; but both these writers gave a very prominent place to faults in the material; thus the third and fourth causes of Paré were, "abundance of seed and overflowing matter, and the same in too little quantity and deficient"; whilst Licetus referred to such conditions as "defect of proper material," "inaptitude of the material," "feebleness of the formative or separative faculty," and the like.

It is unnecessary to quote further from the writers of this century (the seventeenth), for in all of them the same ideas are reproduced,—often, however, with a great deal of obscurity, and not uncommonly in language which now has to us little or no meaning at all. The embryological discoveries of the second half of the century (*e.g.* those of Harvey) so altered the notions of generation which had prevailed that the old teratogenic theories founded upon them fell to the ground. As we shall see later, their place was taken by new hypotheses, which in not a few instances embodied the notions of the ancients; and it came to pass that instead of talking of excess or defect or alteration of the semen, the menses, and the materia, teratologists began to theorise regarding faults in the spermatozoa, in the ovum, or in the product of their union, the embryo.

C. HYBRIDITY AS A TERATOGENIC CAUSE.

The theory which has now to be considered might quite well have been discussed with the preceding, for it has to do with conditions affecting the male and female elements in generation; but it has at the same time very characteristic features of its own, which serve specially to differentiate it. It may be termed the *hybridity theory* of teratogenesis, and it is founded upon the notion that animals of different kinds may be fertile with one another; the products of such unions are, however, monstrous. It was only an expansion of this doctrine to believe that deformed infants resulted from the cohabitation of the human subject (male or female) with one of the lower animals.

"That which followeth is a horrid thing to be spoken; but the chaste mind of the Reader will give me pardon, and conceive that, which not onely the Stoicks, but all Philosophers, who are busied about the search of the causes of things must hold, That there is nothing obscene or filthy to be spoken." Thus wrote Paré (Johnson's *Translation*, p. 599, London, 1678) some three hundred years ago in his chapter entitled, "Of monsters by the confusion of Seed of divers kinds"; and although we must agree with him in theory, yet in practice it will be wise to skim lightly over the surface of the quagmire of offensive and unprofitable imaginings which has collected round the central notion of the teratogenic fertility of different kinds of animals. We do not wish to be miserably quagmired among these teratogenic theories of the past; we desire to reach as soon as possible the comparatively solid land on which have been reared the theories of the present. Let us skirt the quaking bog.

The finding of an anencephalic human fœtus (Geoffroy Saint-Hilaire, *Ann. d. sc. nat.*, vii. 357, 1826) preserved as a mummy in a sarcophagus reserved for sacred animals at Hermopolis, on the Nile, proves that in ancient Egypt the bestial origin of monstrosities was a common belief. The anencephalic fœtus had evidently been regarded as a monkey, an animal sacred in the eyes of the Egyptians, and having been the offspring of a woman, its conception had, doubtless, been ascribed to an act of unnatural intercourse. Possibly the same views held also in ancient Chaldea; at any rate, the cuneiform tablets of Nineveh speak of a ewe giving birth to a lion, etc. (*Teratologia*, i. 139, 1894). It is easy to understand how such beliefs arose when it is remembered that, at the time, all kinds of animals, including man, were supposed to be fertile with one another, and that the male was regarded as the sole factor in generation.

In the mythology of nearly all the races of mankind traces are to be found of similar notions. In the legends of the Greeks and Romans, for instance, mention is often made of the Minotaur, "semibovemque virum, semivirumque bovem"; of Echidna and Chimæra, offspring of Medusa; of Chiron the Centaur, half a man and half a horse; of Castor and Pollux; and of many others. But the conception of half-human monstrosities was not an attribute of the gods of Olympus only; it was a faculty shared in by the humblest of mortals, as is witnessed by the tale which Plutarch (Berger de Xivrey, *Traditions tératologiques*, p. 34, Paris, 1836) tells of Periander's shepherd and the centaur-like offspring of a mare. This same writer attributed to Aristotle the story of the beautiful daughter of Aristonymus of Ephesus, whose name was Onoscellis, which name suggests clearly her asinine origin.

This reference leads us naturally to the consideration of Aristotle's views upon the subject of hybridism. He (*De generatione animalium*, lib. ii. c. 12) held that animals were only fertile with each other when the duration of their gestation-period was the same and when their size was similar. The offspring would resemble either of the parents. The case of the fox and the dog was cited, and Aristotle elsewhere (*De animalibus hist.*, lib. viii. c. 27) spoke of the products of the intercourse of heterogeneous animals in Libya, Cyrene, and Laconia. In this relation, as in so many others, Aristotle's more correct views were soon lost; and Pliny (Holland's *Translation*, i. p. 157, London, 1601), for instance, speaks of a bondwoman who brought forth a serpent, and of Alcippe, who was delivered of an elephant, "marie that was a monstrous and prodigious token, and foreshewed some heavie fortune that followed after."

It is easy to imagine how such beliefs as those mentioned above grew and flourished in the period of intellectual darkness in Europe. Many traces of this are to be found in the writings of Vincent de Beauvais, of Bartholin, of Lycosthenes, of Rueff, of Sir Thomas Browne (*Religio medici*), and others. C. Stalpart vander Wiel, for instance, in his *Hondert seldzame Aanmerkingen*, pp. 234 and 248, Amsterdam, 1682, not only relates how a woman gave birth to a little dog ("Hondeken van een Vrouw geboren"), but even figures the prodigy, which seems really to have been a human otocephalic fœtus without a lower jaw.

With the revival of learning came attempts, not very active at first, to controvert the doctrine of the bestial origin of monstrosities, and the ancient views of Aristotle came again to the front, that animals could only be fertile with those of the same size whose period of utero-gestation was approximately of equal length. Martin del Rio (*Disquisit. magicarum*, lib. ii. quæst. 14, p. 331, Lovani, 1598–1600), a writer of the early part of the seventeenth century, while declaring that physically a cow could not give birth to a human fœtus, was yet of opinion that something of this kind could happen through a diabolic agency. Licetus (*De monstris*, lib. ii. c. 68 *et seq.* pp. 213–231, 1668), however, in five chapters in the second book of his work, opposed the doctrines of Del Rio, and endeavoured by copious references to cases, and by analogy with the vegetable kingdom, to prove that such unnatural unions may not only result in the birth of a human fœtus or an animal, but also in the production of monstrous forms partaking of the characters of both. Neither the legal nor the theological side of this matter were neglected by the writers of this century, and the question whether such offspring ought to be baptized caused much discussion.

Even near the close of the seventeenth century evidence is not wanting to show how persistent was the belief in this mode of origin of monstrosities; for instance, Paullinus (*Miscell. curios. med. phys.*, Dec. ii. Ann. 6; Appendix, obs. xli. p. 48, Norimbergæ, 1688), in 1688, gravely writes of a "Monstrum canino-humanum cum flamma et fragore natum"; and Bartholin tells of a "puella ex cane nata" (*Hist. anat., Cent. V.*, p. 166, 1661). It is true that Ambrosinus, in his edition of Aldrovandus' *Historia Monstrorum* (p. 385, Bononiæ, 1642), had brought in other factors, such as the influence of the maternal imagination, to explain such births; but his suggestions do not seem to have been taken up very widely.

It is not till the beginning of the eighteenth century that we find a strong protest being made against the belief in the hybridity theory of teratogenesis. Bianchi (*De naturali in humano corpore, vitiosa morbosaque generatione historia*, pt. ii. p. 238, 1741), of Turin, was amongst the first to point out that when the product of human gestation had a rough resemblance to an animal-form this resemblance might be due to a fœtal disease, or the product itself might be a mole or retained portion of the placenta. Even at the present day, however, there still exists a strong popular belief in the old theory, and even in the ranks of the profession I have met with its adherents.

Now, there can be no doubt that the cases which gave rise to this belief and kept it in existence were those in which disease or deformity gave to the human fœtus an animal appearance, or in which the young of one of the lower animals, through the existence of such a condition as hydrocephalus, came to bear a rough resemblance to the human form. At the same time, the theory has a modern and scientific side, of which a great deal may yet be heard. To quote from such a skilled teratologist as Mathias Duval (in Bouchard's *Traité de pathologie générale*, i. 159, 1895), writing as recently as 1895, hybridity is a phenomenon of which little is known in the higher forms of animal life, but some day its discussion may form an important chapter in teratology; for it is quite possible that sterility between animals of different species may be due, not to an absence of impregnation, but to such an abnormal development subsequent to impregnation as to cause arrest by its very abnormality. In support of this it has to be noted that Guyer, in an article on the "spermatogenesis of normal and hybrid pigeons" (*University of Cincinnati Bulletin*, No. 22, s. 2, iii. p. 1, 1900), states that he found marked abnormalities in the spermatozoa and germ cells in the pigeons that were crosses between very divergent species; these birds were sterile; in the fertile birds the only changes found were anomalies in mitosis in the cells.

Such, then, were the theories of the past, which regarded purely physical conditions as the causes of monstrosities; and with regard to them all it must be noted that the ideas underlying them exist still, but in an altered form, and expressed in different words. It will have been noticed also that there exists a much closer connection between these theories of the past in their earliest form and the views of the present, than between the latter and the notions of the Middle Ages. The theories of Empedocles and Aristotle are, in other words, more nearly allied to those now in vogue than are the latter to those of Lycosthenes, Licetus, and Aldrovandus. I have regarded the discovery by means of the microscope of the human ova and spermatozoa as the boundary line between what are called theories of the past and those which I shall have soon to describe and designate theories of the present; but there can be no hard-and-fast dividing line in this matter, and it becomes an interesting subject for speculation to consider in what way the knowledge obtained from the use of the microscope might have influenced the teratogenic views of the early Greek philosophers.

I have now passed in review both the supernatural and the physical teratogenic theories of the past; and, before proceeding to the discussion of another old yet ever new theory,—that, namely, of the effect of the imagination of the parents upon the infant in utero,—it must be pointed out that these hypotheses have not followed one another in chronological order, but have existed, more or less side by side, and have even overlapped. For example, a belief in the teratogenic powers of the stars has been seen combating the notion of the hybrid origin of malformed infants, and this in its turn has been confronted with the view that the powers of evil are the potent factors in teratogenesis. At the same time, it is easy to understand how in certain epochs of the world's history certain opinions have been more widely held and more strongly insisted upon than in others.

CHAPTER IX

Teratogenesis (*cont.*): Theories of the Past (*cont.*): Mental Impressions as a Cause of Monstrosities: History of the Theory among the Hebrews, the Ancient Greeks, the Romans, Jews, and Christian Fathers; in the Middle Ages; in the Sixteenth Century; in the Seventeenth, Eighteenth, and Nineteenth Centuries; at the Present Time: Summary.

Theories of the Past (*continued*).

III. THE MENTAL.

DOUBTLESS some modern writers may be inclined to cavil at the position which is here assigned to the theory of the influence of the maternal imagination in teratogenesis, for it is placed with the notions of the past, and not with those of the present. But I think that the arrangement is warranted, for it must be admitted that the theory of maternal (or paternal) mental influence as originally enunciated is indefensible. At the same time, the belief has a modern side, infinitely less repulsive to the scientific sense of inquiry; this side has, I believe, a just claim to credit. The hypothesis as originally stated is, I humbly think, untenable; it is truly a theory of the past. In its modern form, and with certain limitations to be referred to later, it is both tenable and credible; in this sense it can be properly termed a theory of the present. Still, when reference is made to the maternal impression theory in teratogenesis, probably there is scarcely any one who thinks of it in any sense save in that old and extravagant one which demands belief in an absolute similarity between the thing producing the impression and the defect or anomaly resulting therefrom. In its generally accepted and classic sense, therefore, the hypothesis is of the past; but, like others of these ancient doctrines, it has its less widely known but vastly more reasonable modern development. In accordance with these circumstances, it has been placed among the theories of the past, but in juxtaposition with those of the present.

As will be made abundantly evident, when the history of the belief in maternal impressions comes under consideration, the notion is one of great antiquity; but it may here be pointed out that it is also one of practically world-wide distribution. Ploss (*Das Weib*, 2nd edit., i. 505, 1887) has succeeded in gathering together indications of its existence in such far apart lands as India, China, South America, Western Asia, and East Africa; and I have elsewhere (*The*

Diseases of the Fœtus, i. pp. 30, 31, 41, 1892) quoted from various works to show that maternal impressions are not unknown among the Esquimaux, the Loango negroes, and the old Japanese. It is also, of course, the common possession of the nations of Europe. In fact, it may safely be postulated that the belief in the potency of maternal impressions has a geographical distribution corresponding with that of the human race, whilst in the matter of antiquity it is coeval with it.

It will now be well to trace so far as is possible the origin and growth of this ancient and well-nigh universal doctrine. In this way it will be learned that in its earliest beginnings it was not specially a teratogenic theory, but rather one used to explain how the young of men and of animals came to be of special colours, and especially of a tint differing from that of their parents; then it was accepted as the solution of the origin of mother's marks or nævi; then as a possible explanation of the birth of infants with hypertrichosis; and, finally, it came to be applied, and in most ingenious ways, to account for almost every kind of anomaly, malformation, and monstrosity. The story will be found to be one of no little interest, and at times amusing.

Among the Hebrews.

Writers have generally commenced the history of maternal impressions with a reference to the patriarch Jacob and his triple artifice, by means of which he acquired a large number of speckled cattle of a vigorous breed. The sacred narrative tells (Genesis xxx.) how Jacob first placed "rods of fresh poplar, and of the almond, and of the plane tree," in which he had "peeled white strakes," before the flocks when they conceived at the water-troughs, "and the flocks brought forth ring-straked, speckled, and spotted"; having thus obtained some parti-coloured lambs, he put them (instead of the rods) before the flocks, and thus increased the number of such animals still more; and, finally, in order to get as vigorous as possible a breed of the parti-coloured, he put the peeled rods before only the stronger of the flock. "And the man increased exceedingly, and had much cattle, and maid-servants, and men-servants, and camels, and asses." From this it may be learned that Jacob was an expert stock-raiser well versed in all the notions of the age, which included a belief in the efficacy of maternal impressions upon the offspring at the time of conception. To attempt, as many have done, to use the narrative as a proof of the correctness of this ancient theory is manifestly unfair, for throughout the whole passage there is the thinly veiled suggestion of an overruling Providence acting favourably to Jacob's plans.

In Ancient Greece.

Traces of this belief are also to be found in certain of the Greek writers, and Plutarch (*De placit. philos.*, lib. v. c. 12; cited by T. Fienus in his *De viribus imaginationis*, p. 217, Lugd. Batav., 1635) states that Empedocles had remarked that women gave birth to infants resembling the statues which they had found pleasure in regarding during pregnancy. Allusions to the effect of pictures and statues seen by women at the time of conception or during gestation are to be found also in the law of Lycurgus, which required the Spartan wives to look upon the representations of the strong and beautiful, *e.g.* statues of Castor and Pollux; and in the story of Dionysius of Syracuse, who hung the picture of Jason in full view of his pregnant spouse (T. Fienus, *loc. cit.*). There is, however, no absolute proof that Hippocrates shared in these beliefs, for the story which St. Jerome and others tell concerning the use he made of this notion in the defence of a woman accused of adultery is not to be found in the Hippocratic writings (Ballantyne, "Antenatal Pathology and Heredity in the Hippocratic Writings," *Teratologia*, ii. 279, 1895). Further, the statement that "if a pregnant woman has a longing to eat earth and coals, and eats of them, the infant which is born carries on its head the mark of these things," occurs in the treatise *De Superfœtatione*, which practically all commentators regard as not the work of the Father of Medicine himself.

AMONG THE ROMANS, JEWS, AND CHRISTIAN FATHERS.

The following quotation from Pliny's *Natural History* (Holland's translation, p. 161) demonstrates that among the Romans a belief in the efficacy of both the maternal and the paternal mind in the moulding of the fœtus was prevalent. The writer speaks of the black child of a white mother, and then goes on to say: "Certes the cogitations and discourses of the mind make much for these similitudes and resemblances whereof wee speake: and so likewise many other accidents and occurrent objects are thought to bee very strong and effectual therein, whether they come by sight, hearing, and calling to remembrance; or imaginations onely received, and deeply apprehended in the very act of generation, or the instant of conception. The wandering cogitation also and quicke spirit either of father or mother, flying too and fro all on a suddaine, from one thing to another, at the same time, is supposed to bee one cause of this impression, that maketh either the foresaid uniforme likenesse, or confusion and varietie." For this reason Pliny thinks that men are more unlike one another than other creatures: "For the nimble motions of the spirit, the quicke thoughts, the agilitie of the mind, the varietie of discourse in our wits, imprinteth diverse formes, and many markes of sundrie cogitations; whereas the imaginate facultie of other living creatures is unmoveable, and alwaies continueth in one, in all it is alike, and the same still in everyone, which causeth them alwaies to engender like to themselves, each one in their severall kind."

Galen (*De theriaca ad Pisonem liber*, c. xi.), also, believed in the power of the maternal imagination when influenced by pictures, etc.; and Soranus of Ephesus (Περὶ *γυναικείων παθῶν*, c. x.) spoke of the ape-like children which were born to women who had looked at monkeys at the time of conception. Oppian (Κυνεγετικών, lib. i. v. 358), in his *Cynegeticon,* gave some interesting details concerning the application of the belief in the breeding of horses and doves of particular colours. Such statements, however, were not confined to what may be called the scientific literature of the age; for in the well-known romance of Heliodorus (*Æthiopica,* lib. iv. c. x.), the belief is adduced to explain the colour of Chariclea, the white daughter of the black king and queen of Ethiopia, the queen having regarded a statue of Andromeda at the time of impregnation. It may be mentioned that Quintilian, in his *Institutiones Oratoricæ,* referred to a similar tale, only in this instance the parents were white and the infant black, and the cause was the picture of a Moor.

In the Talmud (for Talmudic references, *vide* J. Preuss, *Berlin. Klinik,* Hft. 51, 1892), also, such stories are repeated, and there is an indication of a belief in the potency of impressions made in pregnancy *after* conception. The early Fathers of the Christian Church held similar opinions. St. Jerome thought there was nothing strange in the infant bearing the impress of things seen or imagined at the moment of conception; and St. Augustine, in his *Quæstiones in Genesim,* referred to the biblical narrative of Jacob and his particoloured lambs.

IN THE MIDDLE AGES.

Between the fifth and the fifteenth centuries little is recorded of the belief in maternal impressions, although it cannot be doubted that it existed. It would seem that Marcus Damascenus gave origin to the oft-repeated tale of the birth of a hirsute infant consequent upon the mother regarding the picture of John the Baptist in his hairy garment. St. Isidore, also, seems to have warned women against looking at monkeys, cynocephali, etc., during pregnancy. The Arabian physicians had little to say on the subject, but Avicenna laid stress upon the belief that infants resembled in colour, etc., the things seen by the parents at the time of conception; and gave credence to the ridiculous story of a hen sitting upon her eggs being frightened by a kite, with the result that the chicks had heads like falcons.

From what has been said, it will have been gathered that prior to the fifteenth century the notion of maternal impressions was a well-established one; but it is noteworthy that it does not seem to have been much employed to explain monstrosities, unless indeed we regard the abnormal colour of the skin, nævi, and hypertrichosis as teratological. Further, its efficacy, save at the moment of conception, was not widely recognised; indeed, there is only slight evidence to prove that it was ever supposed to be active in later pregnancy. Its existence, however, was admitted both in the human species and in some of the lower animals, and we read over and over again of the great influence of pictures and statues. The mental impression seems most often to have been one of admiration; rarely is the idea of fear or disgust hinted at.

With the Revival of Learning in Europe came a great extension of the doctrine of the influence of the maternal fancy (phantasia), or, as it was often called, "imaginatio gravidarum," "Einbildungskraft," and (more popularly) "Versehen."

In the Sixteenth Century.

In a work on the "imagination," by Francisco Pico of Mirandola (*Liber de imaginatione*, Venetiis, 1505), published in the early years of the sixteenth century, no mention is made of any peculiar properties of the fancy in pregnant women; and Taruffi (*Storia della Teratologia*, i. 231, 1881) is of opinion that the omission indicated that the author discredited the belief, not that he was unaware of it. Whether this be so or not, Martin Luther, in his work on Genesis, regarded the notion as a "res certa et conveniens cum doctrina medicorum"; he also told a story about a pregnant woman who was frightened by a mouse. Lycosthenes (*Prodigiorum ac Ostentorum Chronicon*, p. 445, Basileæ, 1557) indicated the popular belief when he related how in the year 1282 an infant was born with hair and claws like a bear, and how the Pope of the time straightway ordered the destruction of all pictures of bears in Rome. The child belonged to the well-known family of the Ursini. It may be noted that this story was frequently repeated by subsequent writers, who, however, did not all see in it an instance of such an innocent cause as the mother's imagination. Both Cardan (*Opera omnia*, "De sanitate tuenda," lib. i. c. 9, 1663) and Porta (*Magiæ naturæ*, lib. ii. c. 23, Neapoli, 1558) were firm believers in the theory that, if a pregnant woman longed for anything and touched a part of her body, the fœtus would show a mark of the thing desired on the part corresponding to that touched by the mother (*chirapsy*). They also ventured an explanation to the effect that the spirit of the mother is united with that of the infant, and the heat, which is the instrument of the spirit, moves the blood (which is at once disturbed by the desire of the mother) into the corresponding part in the fœtus. Luiz Mercado (*De mulierum affectionibus*, lib. iii. c. vii., Valladolid, 1579), a Spaniard, had another theory of the *modus operandi*, for he thought that the imagination disturbed the action of the semen of one of the parents, and so led to the mark on the infant.

Lemnius (*De miraculis occultis naturæ*, lib. iv. c. 18, 1564), in his interesting work, stated his preference for the doctrine of the maternal imagination over that of stellar influence; and Ambrose Paré (*De monstres*, Paris, 1573), in 1573, gave it as the fifth cause of monstrosities, mentioning the illustrative instances of black and hairy children already so often referred to. The latter writer also figured an infant with the face of a frog, which Bellanger, "a man of an acute wit," regarded as occasioned by the mother's holding a frog in her hand just before conception. Paré went on to say (I quote from Johnson's translation, p. 596): "There are some who think the infant once formed in the Womb, which is done at the utmost within two and forty days after the conception, is in no danger of the Mother's imagination, neither of the seed of the Father which is cast into the

Womb, because when it hath got a perfect figure it cannot be altered with any external form of things; which whether it be true or no, is not here to be inquired of: truly I think it best to keep the woman all the time she goeth with child, from the sight of such shapes and figures." Cautious Paré!

It is scarcely necessary to do more than mention some of the other references to maternal impressions found in the literature of the sixteenth century. Sebastian Munster (*Cosmographie universelle*, lib. iii., Paris, 1575), for instance, tells how two women, one of them being pregnant, got their heads knocked together, and how in due time twins united by the vertices were born to one of them. J. Rueff (*De conceptu et generatione hominis*, lib. v. c. 3, p. 46, Frankforti ad M., 1580) speaks of the grievous effects of terror induced by the sight of hares and other animals, and says: "Ex appetitu rursum et terroribus multi nascuntur, qui varias maculas et figuras corpori impressas habeant, puta, crinium, murium, variorum colorum, racemorum, flammarum, fructuum, rerumque aliarum." Jean Wier (*De præstigiis dæmonum*, lib. iv. c. 18, Basileæ, 1563) and Cornelius Gemma (*Cosmocritica*, Antwerpiæ, 1575), and several others, participated in the popular belief, which even found its way into the non-medical literature of the time: witness the story of black parents and a white child in the twelfth canto of Tasso's "Jerusalem Delivered." This was indeed the age of the wonderful, and nothing seems to have been regarded as incredible. Profound indeed were the discussions regarding the cutting of a golden tooth by an infant in Silesia, in which Horstius (*De aureo dente maxillari pueri Silesii*, 1595), Ingolstetter (*De aureo dente Silesii pueri*, 1596), and Ruland (*De dente aureo pueri Silesii*, 1597) took part; and in Weinrichius' quaint work entitled *De ortu monstrorum commentarius* (c. 17, p. 158, Breslæ, 1595) we read at great length concerning "*το φαντασικον*" and its supposed effects, about "fœtus ranæ facies," about "infans facie cadaverosa," and so on.

In the Seventeenth Century.

In the succeeding century (the seventeenth) the belief in the teratogenic powers of maternal impressions reigned supreme. Scarcely a writer ventured to throw a doubt upon its accuracy, and the most far-fetched explanations of monstrosities and deformities were eagerly accepted by both the public and the profession. Credulity would indeed seem to have reached a maximum when it began to be asserted and believed that conception might occur through the imagination alone. Of course, little was at this time known of the physiology of generation and of intrauterine life, else such assertions could scarcely have been entertained. Interesting instances illustrating this extraordinary development of the imagination theory were reported by Thomas Bartholin (*Hist. anat. et med. rar., Cent. V. and VI., hist.*, 61, p. 296, Hafniæ, 1661), G. C. Petrus (*Miscell. curios. phys.-med.*, Ann. ii. obs. ciii. p. 303, Jenæ, 1671), and E. S. Grass ("Conceptus prodigiosus," *Miscell. curios. phys.-med.*, Dec. ii. Ann. x. obs. lvi. p. 102, Norimbergæ, 1692). In the first of these we read how Magdalena of Auvermont gave birth to an infant although her husband had been absent from her for four years; and how the occurrence was explained by the fact that the lady had in her dreams imagined her husband to be present; and so the child (Emanuel) was conceived "sola imaginationis virtute." After matrons and medical men had given their evidence upon this matter, the Parliament of Grenoble in 1637 declared the child to be the legitimate son and heir of Hieronymus Augustus of Montleon, the husband of the aforesaid Magdalena.

Even in this credulous age, however, reports of cases like the above were rarities. Most authors were content to narrate how an already existing fœtus was altered; few had the courage to describe the creation of an embryo through the force of the imagination alone. Certain of the records of the time may here be briefly referred to.

In 1605 Riolan (*De monstro nato Lutetiæ anno Domini*, 1605, "Disput. philos.," Parisiis, 1605), in connection with a case of double fœtus, referred to the imagination theory, stating his preference for it over the competitive notion of Satanic influence; the birth of a child resembling a demon was not due to the activity of an incubus, but to the influence upon the mother of pictures of diabolic creatures. Doubtless the women of that day were, or ought to have been, glad to welcome this change in the teratogenic doctrines of the time, for the substitution of the maternal-fancy theory for that of Satanic or bestial intercourse rendered the birth of a malformed fœtus a misfortune, but not any longer a crime. Riolan also believed that while the imagination could alter the properties of the uterine contents, it could not change the species. Fienus (*De viribus imaginationis tractatus*, Quæstiones xiii. to xxiii., Louvain, 1608), in his treatise on the powers of the imagination, devoted more than 150 pages to the discussion of maternal impressions and the various questions arising therefrom; but that he did much to clear up these matters can hardly be asserted. He related the story told by Philippus Meurs about the child with a mussel for a head, who nevertheless lived for eleven years, receiving liquid nourishment from a spoon into the gaping bivalve; of course the mother had longed for sea-mussels in her pregnancy. Concerning this extraordinary maid and her still more wonderful death (through the breaking of one of the shells), Fienus said "dico me non credere"; but he did not hesitate to accept many other marvellous tales. Sir Thomas Browne, it may be noted, does not discuss maternal impressions in his *Vulgar Errors*.

Septalius (*De nævis*, Dordrechti, 1650) and Hildanus (*Observ. et cur. chirurg.*, *Cent. III.*, obs. 56, Francofurti, 1646) also wrote upon maternal impressions; and Schenkius (*Monstrorum historia memorabilis*, Francofurti, 1609) and Bauhinus (*De hermaphroditorum monstrorumque partium natura*, 1614) frequently adduced them to account for various monstrosities. Licetus (*De monstrorum natura*, etc., lib. ii. c. ix., xi., xix., etc., Patavii, 1616), although holding more advanced views on antenatal pathology, yet clung firmly to the theory of the mother's imagination in teratogenesis; but he restricted its power in certain directions, and did not believe that mutilated monstrosities and those showing excess of parts could be thus produced. He admitted the efficacy of the paternal imagination also (lib. ii. c. xlii.); but this could not be so powerful as the maternal, for the time of its action was limited to the venereal act.

It has been pointed out by Taruffi (*Storia della Teratologia,* i. p. 234) that Zacchia (*Quæstiones medico-legales, in quibus,* etc., i. lib. vii., Romæ, 1621), writing in 1621, had indicated weak points in the doctrine of the maternal imagination when he stated that if such things were true, then there would be no infants without marks, and some children would be spotted all over like leopards; but these arguments seem to have fallen on deaf ears, a fate which also met Santorelli's (*Antepraxis medica,* lib. ii. c. xiii. par. 35, Neapoli, 1651) statement, made thirty years later, that monstrosities were born to women who had experienced no impression whatever. Whilst, however, one is willing to give to these Italian observers credit for critical views regarding the popular theory of their time, it must be confessed that their notions found little or no support till many years had passed. The writers who immediately followed held an almost unquestioning faith in the potency of the mother's imagination; and reference may here be made to Aldrovandi's work (*Monstrorum historia,* p. 384, Bononiæ, 1642) and to that of Stengelius (*De monstris et monstrosis quam mirabilis,* etc., p. 179, Ingolstadii, 1647), in both of which the matter is dealt with. Of course these authors recognised not only this but also many other theories of teratogenesis.

Towards the close of the seventeenth century, observations on the supposed results of the mother's fancy multiplied enormously. Thus Kerkring ("Monstrum cacodæmonis picturæ, quam humanæ figuræ similius," *Spicilegium anatomicum,* obs. xxiii. p. 56, 1670) puts on record the birth of what was evidently an anencephalic fœtus, but whose appearance, taken in conjunction with the mother's history, led the midwives to call it a devil—"diabolum non hominem esse conclamitant mulierculæ." He also told of a woman whose occiput was fractured in her pregnancy; the infant's head had no occiput. Swammerdam (*Uteri muliebris fabrica,* p. 29, Leidæ, 1672) opened up new ground when he narrated how a clever woman counteracted her own impression: she saw a negro in her pregnancy, and to prevent her child being black she washed herself in warm water; the matter turned out well, for the infant (who, by the way, was born with teeth) was white save between the fingers and toes and in the grooves on the face, places which the mother in her washing had evidently neglected.

One of the most frequently quoted stories of maternal influence upon the fœtus in utero is that taken from Malebranche's work (*Recherche de la vérité,* lib. ii. c. 7, Paris, 1674), in which it is stated that a pregnant woman after having seen a criminal broken on the wheel, gave birth to an idiot boy, whose limbs were fractured. He also wrote of a woman who from much gazing at a picture of St. Pius was delivered of an infant closely resembling the saint. "'Tis what all Paris may have seen as well as I, since it has been for a long time preserved in spirits of wine." With regard to the first of these tales, Malebranche had no difficulty in explaining all the phenomena to his own satisfaction. "Children," said he (to quote from Blondel's translation), "see what their Mothers see, they hear the same Cries, they receive the same Impressions of the Objects, and are moved by the same Passions. All the Blows given to the Malefactor did violently strike the Mother's Imagination, and, by a Counter-blow, the tender and soft Brain of the Child. The Fibres of the Child's Brain, not being able to resist the Torrent of the Spirits, were broken: That's the Reason why he came into the World without Understanding. The violent Course of the Mother's animal Spirits went, with Force, from her Brains to the several Parts of her Body, which answered to the Parts of the Malefactor. 'Twas the same in the Child, but because the Bones of the Mother were capable to resist the Violence of the Spirits, they were not wounded. Perhaps she did not feel the least Pain; but this rapid Stream of the Spirits was capable to carry away the soft and tender Parts of the Bones of the Child." This sad result would have been avoided had the mother known and practised Malebranche's instructions—"si cette mère eut determiné le mouvement de ses esprits vers quelqu' autre partie de son corps en se chatouillant au ce force, son infant n'auroit point eu les os rompus."

Dolæus (*Encyclopedia chirurgica,* Francofurti, 1689) attempted a more physiological explanation of the *modus operandi* of maternal impressions, and held that the image in the mind was involuntarily communicated to the animal spirits, which impressed it upon the fœtus by means of the nerves of the uterus. The movements of the heart and intestines proved that the animal spirits were capable of involuntary motion. This theory was accepted by other writers, among whom was Bandiera ("Delle voglie che s'imprimono nel feto," *Galleria di Minerva,* iii. pt. 4, p. 101, Venezia, 1695), who, however, by bringing in the paternal imagination, which, of course, can only act at the time of conception, rather stultified the notion, for there is no nervous connection at that epoch.

The remaining contributions of this century may now be summarised. Bayle (*Dissertationes medicæ,* Diss. iii. p. 116, 1678) dealt with the matter of maternal impressions, and regarded it as an endless task; Boyle (*Exper. Philos.,* p. 151) repeated a tale about a speckled child whose mother had (before pregnancy!) gazed long and earnestly at some red pebble-stones near St. Winifred's Well,—and yet his mind conceived Boyle's Law of the relation between volume and pressure! Diemerbroeck (*Opera omnia, Anat.,* lib. i. c. 28, p. 165*b*, Utrecht, 1685) was so sure of the theory that he employed it in his scheme of heredity; and Fidelis (*De relationibus medicorum,* lib. iii. c. 4, p. 405, 1674) used it to explain why deformed parents had not always deformed children. In the pages of a periodical called *Zodiacus medico-gallicus,* Nicolas de Blegny (i. pp. 61, 62, Geneva, 1680) and Cuchotius (v. p. 249, Geneva, 1685) recorded further instances of maternal impressions. Finally, the volumes of the *Miscellanea curiosa* are full of cases of fœtal monstrosities ascribed to the influence of the mother's mind and imagination. Amongst these may be mentioned the contributions of Ludovici (Ann. iv. and v. obs. 208, 1676), Segerus (Ann. iv. and v. obs. 147, 1676), Mercklinus (Ann. viii. obs. 46, 1678), Sommerus (Dec. ii. Ann. i. p. 113, 1683), Albrecht (Dec. ii. Ann. vi. obs. 14, 1688), Fehrius (Dec. ii. Ann. vi. obs. 30, 1688) Göckelius (Dec. ii. Ann. vi. obs. 126, 1688), Hoffmannus (Dec. ii. Ann. viii. p. 483, 1690), Lentilius (Dec. iii. Ann. ii. obs. 117, 1695), and Reiselius (Dec. ii. Ann. ii. p. 272, 1684).

In the Eighteenth Century.

In the seventeenth century the attitude of the profession towards the doctrine of maternal impressions was one of blind credulity; but in the eighteenth this was quickly changed for one of sceptical criticism. Of course, there were still many who in the latter century believed in the efficacy of the mother's mind in moulding the unborn infant; but the prevailing opinion was one of grave doubt. It would have been strange indeed if this had not been so, for the discoveries of the close of the seventeenth century had done much to clear up many of the vexed questions of reproduction and antenatal physiology.

In the early years of the century, criticism was not yet rife. Düttel (*vide Teratologia*, i. p. 41, 1894), for instance, in his work on fœtal diseases, clearly stated his views: "So great," said he, "is the sympathy between mothers and the fœtuses which they carry in the uterus that they suffer closely with them, to such an extent that not only are the delicate fibrillæ of the infants excited to anomalous movements by every severe affection of the mind of the mother (*e.g.* sorrow and anger), but, what is more, the formation of parts is altogether prevented, disturbed, or vitiated by the strong imagination of the mind." In the *Miscellanea curiosa* cases of maternal impression continued to be reported; and in England Daniel Turner (*A Treatise on Diseases incident to the Skin*, pt. 1, c. xii., London, 1714) stated very confidently his belief in such occurrences, for after enumerating most of the cases to which reference has been made above, he said: "Thus is it made apparent by a Multitude of Examples, how manifest and great an Empire the *Fantasy* of a pregnant Woman has over the Blood and Humours together with the Spirits of her Body, and how by their Ministry she is able to give not only monstrous Shapes and Figures to that of the more tender *Fœtus*, but to communicate Diseases also." He also related cases from his own practice of a raspberry mark near the eyebrow, of a currant-like excrescence on the internal canthus of the eye, etc. In the year 1726 the matter of maternal impressions was brought still more prominently before the profession and the public in England in connection with the notorious case of an "Extraordinary Delivery of Rabbets," which was alleged to have occurred in the case of Maria Tofts of Godlyman (Godalming) in Surrey; she had had a great longing for "Rabbets" in early pregnancy. Those who are interested in this case will find the details in the books by Sir R. Manningham, T. Braithwaite, C. Ahlers, and N. St. Andre (London, 1726, 1727).

It is probable that the "Godlyman" case, in conjunction with the appearance of Turner's appreciation of the doctrine of maternal impressions, stirred up Blondel (*The Strength of Imagination in Pregnant Women examin'd*, London, 1727) to write his famous criticism thereupon; but already in the year 1712 Nigrisoli (*Intorno alla generazione dei viventi*, p. 5, Ferrara, 1712) had argued against the popular belief, and had pointed out that the fœtus was entirely separated from the mother, that monstrosities occurred in animals in whom they could scarcely be ascribed to imagination, and that in the human subject deformities were met with for which no disturbing impression could be alleged. To Blondel, however, belongs the credit of dealing to the maternal impression theory the most deadly blow it had yet received. Very skilfully did this writer marshal his facts; and with no small degree of humour, and now and then some biting sarcasm, did he state his arguments and refute the assertions of those whom he delighted to dub the "imaginationists." In the first instance, his satire was specially directed against Mr. Daniel Turner; but he did not spare other, older, and more widely known exponents of the imagination theory. The first edition of Blondel's work was published anonymously in 1727, at least on the title-page the author was simply described as "a member of the College of Physicians"; but in the second issue of the book in 1729, in which were many additions and amplifications of the argument, the writer openly avowed himself, not "out of ostentation," as he said, but to show "that I dare face the enemy."

Blondel arranged his facts and arguments with intent to prove that the current theory was unsupported by experience, by reason, and by anatomy. With regard to experience, he showed that impressions often occurred which were not followed by marks or anomalies in the fœtus, and that deformities were met with in cases in which no impression was alleged. Further, he analysed in detail the exceptional cases in which it had been maintained that a definite impression had resulted in the production of a similar mark on the infant; and under such pithily descriptive epithets as "Parey's Frog," "Miss Muscle and the Grenadier," "the Baker bit," "Sir Kenelm Digby's Patch," etc., he subjected to much ridicule the illustrative instances gathered (mostly from Fienus) with great care and apparently with almost perfect faith by Daniel Turner. Having dismissed these, Blondel turned his attention to the story of Jacob and his rods, which curiously enough seems greatly to have exercised him. Most of his readers will agree that he was at altogether unnecessary pains to explain away this particular case. The author concluded that there "are so many odds against imagination that the cases related in its favour can never overbalance those which are against it," and in his opinion they "may be compared to an accidental hit of a dream or the predictions of a Fortune-teller, which, now and then, are accomplished."

Blondel, then, having "entirely beat the Imaginationists out of their Entrenchments of Experience," attempted to show that reason also was against the popular belief. Conception, the growth of the embryo, and the determination of its sex were all outside the power of the mother's will. "How," he said, "can anybody believe, without reflecting upon the Wisdom of God, that it is left to her to disfigure the child, and to spoil the regular Work of Nature?" Again, since the woman cannot by her imagination mark her own body, it does not seem probable that she should be able to act thus on her fœtus. Other arguments were advanced, and then the writer pointed out that there exists no communication of nerves between the mother and fœtus, and so there could be no communication of thoughts, as alleged by Malebranche and others. In his efforts to absolutely extinguish any flickering flames of belief in the imagination theory, Blondel adopted the erroneous doctrine of the pre-existence of all the parts of the fœtus somewhere before conception. By what means, then, can the mother's imagination obliterate the lineaments of the fœtus, which were pre-existent to conception and subsisting ever since the creation of the world? Finally, anatomical reasons are adduced to show that there is no direct circulation of blood between mother and fœtus, and Blondel refers to the much more probable natural causes of fœtal marks, such as intrauterine diseases or traumatism and heredity.

Blondel's work, which I have thus attempted to epitomise, produced a great effect upon medical opinion all over Europe, and soon numbered adherents in nearly every civilised country. In France, for instance, not only did translations of the English physician's work appear, but Bellet also wrote a book to combat the popular belief in impressions (*Lettres sur le pouvoir de l'imagination des femmes enceintes*, Paris, 1745). In Germany, also, Haller (*Opuscula sua anatomica*, p. 150, Göttingæ, 1751) to a large extent threw the weight of his authority into the scale against the popular theory; and, in Russia, Roederer (*De vi imaginationis in fœtum negato*, 1756) did likewise, though with less effect. In Scotland, Alexander Monro (*Med. Essays and Observ.*, ii. 238, Edinburgh, 1734), in his essays on the nutrition of fœtuses, showed clearly that he was an opponent of the maternal imagination theory, for he wrote (in 1734) as follows:—"The Liquors sent into the *Fœtus* by the umbilical Vein not having their propelling Force communicated from the Mother, the State of the Mother's Pulse cannot affect the Child otherwise than by occasioning Abortion, or vitiating the Fluids that are to be absorbed; and therefore we may be convinced, how vain it is to pretend to account in a physical Way for the Impressions said to be made on Children by the Imaginations of the Mothers." Monro's correct views on fœtal physiology, along with their bearing on impressions, seem, however, to have been overlooked by succeeding writers. Vari (*Ragionamento in aggiunta alla Dissertazione del Signor G. Blondel*, p. 175, Ferrara, 1760), in Italy, was at first a supporter of Blondel's position, but afterwards through a personal experience came to change his views. Plancus, another Italian, entirely sided with Blondel.

Whilst, however, the spirit of criticism was thus infused into the subject, there was still in the minds of many authorities a firm belief in the potency of maternal impressions as teratogenic factors. Superville (*Philos. Trans.*, xli. (for 1740), pt. 1, p. 306, London, 1744), for instance, after relating how seven pigs taken from a freshly slaughtered sow all showed the bloody mark of the knife about their necks, proceeded to state his adherence to the theory of the influence of the "disturbed and disordered imagination of females." He referred to certain objections to the belief, and then said: "I own I do not comprehend it neither. It does not follow from thence, that we ought to reject as false all that our Reason cannot penetrate into." Gregory (*Philos. Trans.*, xli. (for 1741), pt. 2, p. 764, London, 1744), writing soon after, seems to have had even less doubt, for he told how a pregnant woman "took prodigious notice" of a monkey with a hood turning on a stick, and how the fœtus in utero turned over and over in like manner (for were there not twists in the umbilical cord?), and when born was seen to resemble closely a hooded monkey. Nicolai (*Gedancken von der Erzeugung des Kindes,* Halle, 1746) tried to refute Blondel's opinions; but had to admit that monstrosities did not resemble the subjects of the impression (1749).

It must also be borne in mind in estimating the influence of the writings of Blondel and his followers that on the Continent the great weight of Boerhaave's authority (*Prælectiones academicæ,* iv. pt. 2, p. 261, Taurini, 1742–45) had been in favour of the old theory, with certain reservations regarding the sort of impression and its mode of incidence. Boerhaave's commentator, Van Swieten (*Commentaria in H. Boerhaave Aphorismos,* iii. pt. 1, par. 1075, Viennæ, 1743), seems to have been much struck by the lifelike representation of a caterpillar on the neck of a young girl whose mother had in her pregnancy been impressed by a real caterpillar crawling on her neck. Another defender of the imagination theory was Krause (*Quænam sit causa proxima mutans corpus fœtus,* St. Petersburg, 1756), whose dissertation obtained special honour at the Imperial Academy of Science in St. Petersburg; he alleged the existence of a nervous communication between the mother's uterus, the placenta, and the fœtus, and had no difficulty in understanding how disturbances of the mother could deform the infant, especially since the organs of the latter were so tender.

Boerhaave, however, was not always so fortunate as to have a commentator willing to accept all his views on the subject of maternal impressions. Albert von Haller (*Elementa Physiologiæ,* viii. lib. 29, p. 129, Bern, 1766), in fact, did much to support Blondel's criticism, whilst he also established it on more scientific arguments. For instance, he maintained that if there existed a nervous communication between mother and fœtus, then the gathering together of the placental nerves in the umbilical cord would constitute so evident a strand of nerve-tissue that no observer could possibly overlook it. If, again, the communication was a vascular one,—and this might be admitted,—how could images of things be transmitted by means of a column of liquid in a tube. The birth of twins of different colour was explicable in a more prosaic manner than by the invocation of the mother's imagination. Nævi, according to Haller, were due to skin disease, and monstrosities were the result of fœtal maladies. It does not appear that this author was altogether opposed to the doctrine of impressions, for he seems to have been struck by the fact that children resemble their parents, and to have regarded it as an argument in favour of the theory. Smellie (*Treatise on Midwifery*, ii., cases 89 and 90, London, 1754), who lived about the same time, was, doubtless, sceptical also; for, after noting two cases, he wrote: "Notwithstanding these examples, I have delivered many women of children who retained no marks, although the mothers had been frightened and surprised by disagreeable objects, and were extremely apprehensive of such consequences."

Morgagni (*De sedibus et causis morborum*, Epist. 48, Venetiis, 1761) was yet another well-known writer of this period who hesitated about throwing overboard the theory of impressions; he believed that while most cases in which a fœtal defect resembled a maternal impression were accidental coincidences, yet some contained another element which he freely confessed that he did not comprehend.

Between the years 1760 and 1780 it ought to be noted that several popular statements of the anti-imaginationist side of the matter were put before the British public in the form of "letters" or "essays" from anonymous authors, addressed to "the ladies" or to "a married lady." In these works the arguments used by the writers to convince their fair readers are often interesting and even amusing. In one, published in 1765, the author says, "a mark which has been foretold has once in 1000 times happened to answer its description; another effect of chance, which may serve to support the prejudice of those who do not reason, but can have no influence on those who, like you, madam, are only convinced by truth." Another author, writing in 1772, sums up as follows: "The same chain of ideas that shows the impropriety of believing the cure of a toothache by a charm; the destruction of warts by turning thief, and stealing raw meat; the cure of the cramp by wearing rosemary, or placing the soals of our shoes uppermost when we go to bed: I say, the same chain of ideas that shows the impropriety of believing these absurdities, will, when applied with a real desire to be informed, whether the imagination in pregnant women possesses the powers ascribed, convince the enquirer that the tales told of the mother's imagination exerted on the fœtus, are a collection of falsities formed by superstition and ignorance, and continued by prejudice and credulity."

The last years of the eighteenth century did little to settle the question of the potency of the mother's imagination on the fœtal form. We find, in fact, that the minds of the writers of the time were greatly exercised with the side question—a theological one—concerning the result which an acceptance of the imagination theory would have upon the idea formed of the Creator of the Universe. To the discussion of this matter Rickmann, Arnold, Engelhardt, and others devoted themselves; but into their arguments it is unnecessary to enter. Other writers, some for and some against the popular theory, were Eller, Kooy, Schönwald, Schenk, Jeunet, Bablot, Hoffmann, Fielitz, and Schumann; but the enumeration of their names must suffice for the purposes of this sketch.

It may be of interest to the curious to know that near the close of the eighteenth century the money value of a maternal impression (of a patriotic kind) was fixed at 400 francs per annum; for Geoffroy Saint-Hilaire (*Histoire des Anomalies*, i. p. 332, 1832) records that in the third year of the French Republic an infant was born with the representation of a Phrygian cap of liberty on the left breast, and to the mother the Government awarded the above sum, presumably for her patriotic thoughts!

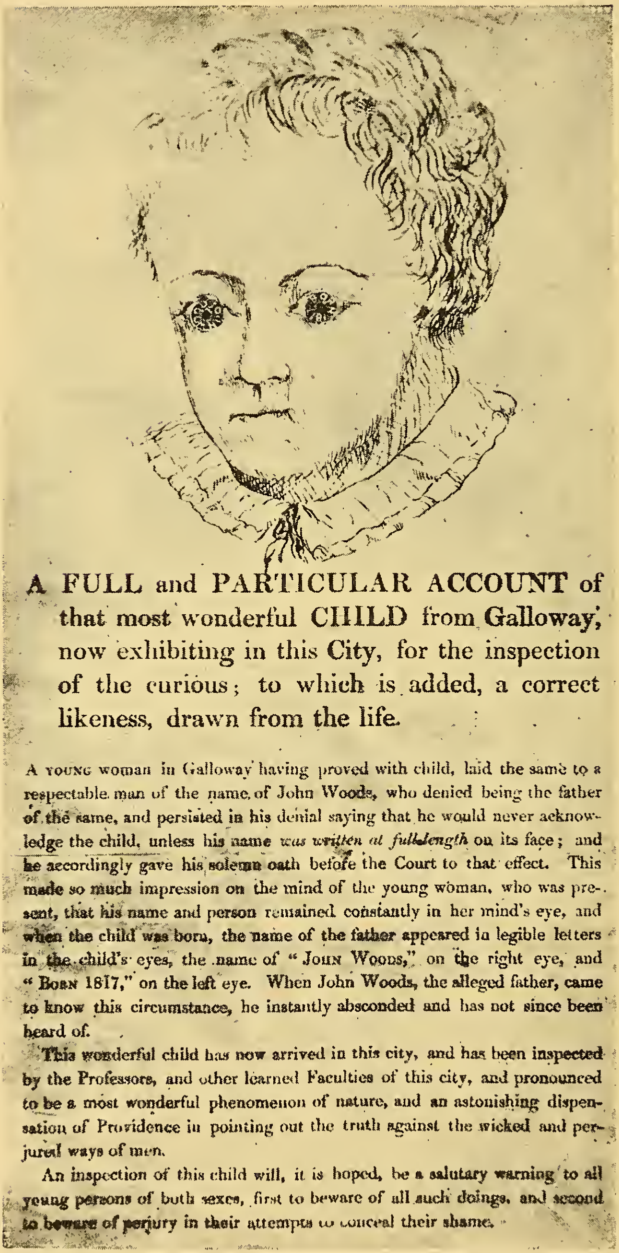
In the Nineteenth Century.

The nineteenth century opened with the question of maternal impressions still unsolved. Medical opinion took one of three lines: complete belief in the potency of a mother's imagination to mark her fœtus in exact resemblance with the object acting upon her mind; or complete disbelief in any such power; or an intermediate line of partial acceptance of the doctrine of maternal mental influence over the infant,—an attempt to reconcile the traditional belief with the spirit of modern scientific inquiry. Popular opinion took a line which is well exemplified by the accompanying illustration (Fig. 22) and the legend annexed thereto. Doubtless the supposed words on the eyes were irregularities in the iris such as have been seen in more recent times by A. Claus (*Flandre méd.*, i. p. 65, 1894) and others.

It now became increasingly difficult for the trained physician to accept the old doctrine, for the researches of the eighteenth century had demonstrated that there was no direct communication between the circulatory system of the mother and that of her fœtus, and in the early part of the nineteenth it became evident that no demonstration of a structural nervous union could be given. On the other hand, the effect of these anatomical discoveries concerning the connection between mother and unborn infant was to some degree discounted by the enunciation of animal magnetism by Mesmer, and its partial acceptance by the medical profession; for, if its tenets were correct, there was no longer any need for the demonstration of nerves in the umbilical cord.

In the first year of the century Desgranges (*Rec. d. actes Soc. de Santé de Lyon*, ii. p. 83, 1801) published his communication in support of the maternal imagination theory, specially in reference to nævi materni, and he has been followed by a long series of writers, some favourable, some inimical, to the doctrine. Besides the authors who have made special contributions to this subject, nearly every one who has written on midwifery, surgery, diseases of children, and dermatology, has ranged himself amongst the believers, the unbelievers, or the neutrals. An enormous literature has, therefore, gathered around the question of the mother and her influence upon her unborn child, and it becomes impossible to do more than point out certain of the more important articles which have dealt with the matter.

If we consider first what the teratologists of the nineteenth century



A FULL and PARTICULAR ACCOUNT of that most wonderful CHILD from Galloway, now exhibiting in this City, for the inspection of the curious; to which is added, a correct likeness, drawn from the life.

A YOUNG woman in Galloway having proved with child, laid the same to a respectable man of the name of John Woods, who denied being the father of the same, and persisted in his denial saying that he would never acknowledge the child, unless his name *was written at full-length* on its face; and he accordingly gave his solemn oath before the Court to that effect. This made so much impression on the mind of the young woman, who was present, that his name and person remained constantly in her mind's eye, and when the child was born, the name of the father appeared in legible letters in the child's eyes, the name of "JOHN WOODS," on the right eye, and "BORN 1817," on the left eye. When John Woods, the alleged father, came to know this circumstance, he instantly absconded and has not since been heard of.

This wonderful child has now arrived in this city, and has been inspected by the Professors, and other learned Faculties of this city, and pronounced to be a most wonderful phenomenon of nature, and an astonishing dispensation of Providence in pointing out the truth against the wicked and perjured ways of men.

An inspection of this child will, it is hoped, be a salutary warning to all young persons of both sexes, first to beware of all such doings, and second to beware of perjury in their attempts to conceal their shame.

FIG. 22.—A "Maternal Impression" story of the beginning of the nineteenth century.

have said on the subject, we shall find a very marked leaning towards the total condemnation of the theory of maternal impressions. Jens Bang (*Abhandlung über eine Missgeburt*, Kopenhagen und Leipzig, 1801), it is true, supported the old doctrine, and Jouard (*Des monstruosités et bizarreries de la Nature*, Paris, 1806) took up an intermediate position; but nearly every one else has showed great scepticism, some even passing the subject over in complete silence. Tiedemann (*Anatomie der Kopflosen Missgeburten*, par. 88, p. 100, Landshut, 1813), in his work on acephalic fœtuses, pointed out that only in one case was an impression recorded; further, he insisted that the fact that one twin was commonly normal whilst the other was so deformed was a strong argument against the theory; and, finally, he propounded the question, What imagination of the mother could be at work to produce in the infant a one-horned uterus or an intestinal diverticulum? Zimmer (*Physiologische Untersuchungen über Missgeburten*, p. 35, Rudolstadt, 1806) and Clesius (*Etwas für Eheleute, etc.*, p. 40, 1812) also opposed the imagination theory, and Herholdt (*Betragtninger over Misfostere*, 1828) entered at great length into its history. We find Etienne G. Saint-Hilaire ("Monstre" in *Dict. classique d'histoire naturelle*, xi. p. 40, 1827) taking an intermediate position; but he pointed out that prolonged moral impressions could have little or no teratogenic effect, as shown by the very small number of monstrosities born in such a large city as Paris. He also noted three cases in which a sudden and sharp impression was the cause of anencephaly, not through the imagination alone, but on account of the sudden uterine contraction thereby produced, and the consequent pressure on the ovum or embryo. He thought that prolonged emotions might weaken the fœtus without making it actually monstrous. Isidore G. Saint-Hilaire (*Histoire des Anomalies*, iii. p. 540, Paris, 1836) adopted largely the views of his father in this matter; but he more clearly defined the sphere of action of an impression. Violent and sudden impressions may cause monstrosities in the manner above indicated; moderate or feeble, but long-continued impressions may also, it cannot be denied, produce malformed and even monstrous infants; but it cannot be believed that slight and transient desires, feelings of disgust or of fear, etc., have any influence upon the form of the unborn infant. "Il est surtout contraire à toutes les données de la science et de la raison, de croire qu'un objet vu, craint ou désiré par la mère, puisse venir, pour ainsi dire, se peindre sur le corps de l'enfant qu'elle porte dans son sein; et la saine physiologie ne peut voir dans cette ancienne croyance qu'un préjugé aussi absurde, et quelquefois aussi dangereux qu'il est ancien."

Vrolik, another well-known teratologist, was more clearly an unbeliever than were the Saint-Hilaires, for he admitted nothing further than that a nutritive disturbance in the mother following a severe shock might lead to a defective development of the fœtus. Förster (*Die Missbildungen des Menschen*, 2nd edit., p. 4, Jena, 1865) enumerated eight arguments against the impression theory, including the statement that most malformations develop in the first month, nay, even in the first week of pregnancy, and therefore at a time when the mother commonly does not know that she is pregnant. He also noted that impressions were common while monstrosities were rare, that there was no direct nervous communication between mother and fœtus, and that one twin might be normal and the other malformed. Wonderful stories impressed Förster not at all: "die Literatur ist voll von solchen Fällen, noch mehr aber die Köpfe der Hebammen und alten Weiber weiblichen und männlichen Geschlechtes."

Of the more recent teratologists nearly all have treated the subject of the influence of the maternal imagination as a silly fable; and in the works of Ahlfeld and Hirst and Piersol there is no reference to it, whilst in those of Taruffi, Guinard, and Blanc it is simply considered from a historical standpoint. E. Martin (*Histoire des monstres*, p. 266, Paris, 1880), alone, has argued in favour of a modified form of the old belief. He has stated that imagination plays an undoubted part in the procreation of monstrous forms; but he has also insisted that this part is a mechanical one,—that through the nervous system the uterus is thrown into contraction, and thus undue pressure is brought to bear on the embryo. The occasional occurrence of fœtal malformations which resemble the objects causing the maternal nervous disturbance is purely coincidental. Martin seems also to regard the mother's mental state during pregnancy as in some degree modified so as to be more susceptible to impressions.

Alongside of this almost total abandonment of the imagination theory by the teratologists of the nineteenth century, we have to place the extraordinary rejuvenation of the ancient doctrine among the leaders of the medical profession in the United States of America. Between 1839 (the year in which the report of the "Snake-man," Robert H. Copeland, whose mother, when pregnant, had been struck by a rattlesnake, appeared) and 1900, papers dealing with maternal impressions, to the number of 170, were published in American journals. Not only have the contributions been many, but they have also, with few exceptions, been favourable to the imagination theory. Further, amongst those who have most warmly supported the old doctrine were such acute thinkers and weighty authorities as Fordyce Barker (*Trans. Amer. Gynec. Soc.*, xi. 152, 1887), Samuel C. Busey (*ibid.*, p. 176), and William Goodell (*Amer. Journ. Obst.*, iv. 131, 1871). Fordyce Barker thought "that the weight of authority must be conceded to be in favour of the doctrine that maternal impressions may affect the development, form, and character of the fœtus," and even went so far as to believe that "these causes may act effectively on the ovules before fecundation," alleging in proof the famous "Dundreary Case." Barker also included telegony, or the influence of a previous sire, in the sphere of maternal impressions. Goodell was, "to a certain extent," converted from a sceptic into a believer by a case of pre-natal "circumcision" which occurred in his own practice.

It must not, however, be thought that the theory of maternal impressions was unanimously accepted by the profession in the States. On the contrary, J. G. Fisher (*Amer. Journ. Insan.*, xxvi.

241, 1869–70) wrote at length against the popular opinion, but did not add any novel arguments; and Dugas (*South. Med. and Surg. Journ.*, 3 s. i. p. 317, 1866–67), Norman Bridge (*Chicago Med. Journ. and Exam.*, xxxii. 577, 1875), and Conant (*Trans. N. York Acad. Med.*, ii. 267, 1857–63) were all strong in their opposition. Still, it is evident that within recent times the theory has been held strongly by a great many medical men of note on the other side of the Atlantic; for Hubert Work (*Med. News*, lxv. 451, Philadelphia, 1894), writing in October 1894, was able to report that out of thirteen physicians (including Penrose, Goodell, Matthew D. Mann, Hatfield, Cooke, Hirst, W. A. Edwards, and A. T. King) whose opinion he asked, only one (Hatfield) was emphatic in his disbelief of the statement that "pronounced impressions made upon the mind of a pregnant woman predispose to bodily defects and birth-marks in the child."

The trend of opinion in America is also learned from the study of Dabney's contribution to Keating's *Cyclopædia of the Diseases of Children* (i. p. 191, 1889), and from that of Edward P. Davis to Norris' *Text-book of Obstetrics* (p. 213, 1896). Finally, to quote from popular literature, Oliver Wendell Holmes had not a little to say about the result of an "impression" in his fascinating novel *Elsie Venner*. This is by no means the only instance of the belief entering into the fiction of past and present times; for allusions to it are found in Shakespeare's *Merchant of Venice* (Act i. sc. 3), Scott's *Fortunes of Nigel*, and Sterne's *Tristram Shandy*, while from a casual survey of modern literature I have noted references thereto in Blackmore's *Lorna Doone*, in Henty's *Rujub the Juggler*, in Merriman's *From one Generation to Another*, in Egerton's *Keynotes*, and in Cobban's *Red Sultan*.

Whilst the teratologists of the nineteenth century practically abandoned the imagination theory, and whilst American writers in large degree resuscitated the doctrine, surgeons, obstetricians, physiologists, and dermatologists in Europe held very various opinions thereupon. In Germany, for instance, in the first half of the century there were many who wrote on the power of maternal impressions, among whom were Harting, Merle, Klein, Gittermann, Hirsch, Wesener, Schneider, Keyler, Braun, Späth, Kœhler, Pauli, Rubner, Solbrig, Droste, Hoffmann, Straube, and Leopold. All did not support the old belief; but many did so, and some even went to ridiculous lengths, such as to affirm that the infant's feet were deformed by the mother wearing tight shoes in her pregnancy (Schneider, *Ztschr. f. d. Staatsarznk*, ix. p. 37, Erlangen, 1825), and to say that the sight by a woman of a one-armed man at the eighth month of her pregnancy could cause the birth of a fœtus with one arm wanting. Others, such as Jörg and Meissner, argued against the theory, the latter bringing forward some strong clinical evidence. J. Müller, the physiologist, also, was a strong opponent of the theory; but Burdach, another physiologist, supported it, and thought that the relation between mother and fœtus was an occult one, like animal magnetism. In the second half of this century a comparatively small number of German writers wrote specially on the subject (including Brach, Wagner, Ritter, van Praag, Tassius, Willige, Adler, Santlus, Heidelberg, Upmann, Clemens, Roth, Wolff, Preuss, and the text-book writers); but save in the period 1850 to 1860 the general feeling has been strongly opposed to the ancient doctrine.

In France and Belgium the general trend of opinion during the century was much the same as in Germany. Amongst the special writers on the subject must be named Desgranges, Martin, Clarae-Faget, Girard, Levêque-Lasource, Demangeon, Bérard, Burggraeve, Steinbrenner, Guislain, Schoenfeld, Pigeolet, van Camp, Bayard, Turck, Schrevens, Liebrecht, Loin, Liégey, Mijnlieff, Delassus, and Variot. Burggraeve (*Ann. de gynéc. et pédiat.*, 2 s. i. p. 115, Bruxelles, 1840–41) attempted to give a more scientific aspect to the old theory by combining it with the known facts of embryology: he related how a woman at the third month of pregnancy saw a pig with its throat cut, and feared that her infant might be affected; the child showed a cleft in the throat which the author regarded as due to the want of union of the branchial arches which were separate at the time of the impression. Guislain reported (amongst others) a curious case of aural deformity following a "longing," and Bourgeois concluded that "les impressions profondes ou vivaces de l'imagination occasionnent quelquefois chez l'enfant des vices de conformation." In 1876 Liebrecht wrote in support of the theory of impressions; and Delassus (*Arch. de tocol.*, xviii. p. 923, Paris, 1891) related two cases (one of hare-lip and one of anencephaly) which seemed to have confirmed him in his belief in the old doctrine.

In Italy, also, the power of the imagination of the mother in teratogenesis has found defenders and opponents and critics, to some of whom Taruffi (*Storia della teratologia*, i. p. 242) refers. For instance, Monteggia put on record a case of intrauterine amputation alleged to be due to the mother seeing many cases of amputations; Barbieri argued against the belief, and suggested more natural explanations of fœtal states, and Vannoni hinted that possibly a predisposing condition was needed in mother and fœtus before an impression could become efficient. Fenoglio, Viparelli, and others contributed further to the literature of the subject in Italy. In Poland, Neugebauer was a believer, as Drzewiecki (*Med. Rec.*, xl. p. 529, New York, 1891) tells us.

With regard to Great Britain, it would seem that the influence of Blondel, Monro, and Smellie was largely effective in preventing a wide acceptance of the imagination theory in the ranks of the profession. Alleged cases from time to time appeared in the *Lancet* (*e.g.* those reported by Hoare, Canton, Rankin, Wansbrough, O'Shea, Dunn, Beale, Child, Daly, and others); the *British Medical Journal* (*e.g.* those by Curran, Houghton, Graham, Thompson, Clapperton, Huntley, R. J. Lee, Sandham, Jenkyns, Jones, and others); the *Medical Times*, the *Dublin Medical Press*, and the *Glasgow Medical Journal*; but although these contributions were fairly numerous, the feeling amongst obstetrical teachers was inimical to the notion of maternal influence. Ryan (*Lond. Med. and Surg. Journ.*, iv. 170, 1833–34), for instance, was strongly opposed to it, and so have been many others. Montgomery (*Signs and Symptoms of Pregnancy*, 2nd edit., p. 17, London, 1856) was an exception, for he wrote, "I cannot help thinking it quite consistent with reason and the present state of our knowledge to believe that a very powerful impression on the mother's mind or nervous system may injuriously affect the fœtus, still lodged in her womb, actually a part of herself, and deriving its supply of life from her blood; and this, the more especially, as many instances have been witnessed in which the child *after birth* has suffered seriously by being suckled by a woman labouring under some strong mental impression."

The matter was brought up by myself on two occasions (*Edinb. Med. Journ.*, xxxvi. p. 624, 1890–91; xxxvii. p. 1025, 1891–92) at meetings of the Edinburgh Obstetrical Society, with the general result that no decisive proof for or against was forthcoming, and that the question was still to be regarded as *sub judice.* Barnes was content to leave the problem unsolved; but Ashburton Thompson (*Trans. Obst. Soc. Lond.*, xix. p. 94, 1878) would seem to have been a believer. Much more might be said concerning British contributions to this vexed question, but it must suffice to note that Everard Home (*Phil. Trans.*, p. 66, London, 1825) was a supporter of the doctrine.

AT THE PRESENT TIME.

What may be the fate of the theory of maternal impressions in teratogenesis in the twentieth century it is impossible to foretell; but it is safe to say that the diffusion of the views that group themselves around "Christian Science" and "Mind Cures" will strengthen the belief in the power of the mother's imagination to alter the appearance of her unborn infant and so tend still further to raise the idea in popular estimation. A glance at current medical literature will show that the subject is still before the medical profession, although I fancy there are signs that scientific practitioners are becoming more and more sceptical regarding it and more exacting in their investigation of the details of recorded cases. At any rate the articles of H. F. Lewis (*Amer. Journ. Obst.*, xl. 84, 1899) and J. G. Kiernan (*Medicine*, vi. 450, 1901) suggest this conclusion.

Summary.

A survey of the whole history of the belief in maternal impressions leads me to say about it what Sir Thomas Browne said long ago about the common opinion that crystal is nothing else but ice or snow concreted (*Pseudodoxia Epidemica*, bk. ii. c. i., 1646): "Of which assertion, if prescription of time and numerosity of assertors were a sufficient demonstration, we might sit down herein, as an unquestionable truth, nor should there need ulterior disquisition; for few opinions there are which have found so many friends, or been so popularly received, through all professions and ages." But the scientific antenatal pathologist refuses to "sit down herein"!

Such is, in outline, the history of this teratogenetic theory, extraordinary alike whether its truth be affirmed or denied; wonderful alike in its wide extension in space and time, and its firm hold upon the minds of both profession and laity. To those who wish to see it dead it is most disappointingly vital; to those who wish to demonstrate its truth most strikingly destitute of scientific proof. In its support is a marvellous mass of evidence of the *post hoc ergo propter hoc* kind; arrayed against it are the scientific theories of biology which have been gradually and laboriously built up by the savants of this and of other ages.

From the standpoint of the student of antenatal pathology the theory of maternal impressions must be regarded as a great misfortune. Many instructive cases of fœtal disease and deformity have been practically lost to science through the absorption of the observer's mind in ideas of the mental process in the mother which could have caused the state of her infant, and through his desire to trace in the morbid fœtal condition a resemblance, often far-fetched indeed, to some animal, vegetable, or mineral. In this sense the theory has been the grave in which a great deal of fœtal pathology has been buried; for instead of a case being entitled one of anencephaly, or of fœtal ichthyosis, or of hirsuties or hairy nævus, it has been simply labelled "a curious instance of maternal impressions," "a striking case of the influence of the mother's mind on the fœtus," etc. Further, the material thus hidden away is in most cases permanently lost; for a reference to the report usually gives us no anatomical or pathological details to enable us to identify the malady or the malformation, but simply tells us that the infant had a head like a cat or a rat, or was hairy like a bear, or had scales like an alligator or a snake.

The theory has had a maleficent effect on the progress of the study of antenatal pathology. Of that there can be no doubt. But the question whether there is or is not any truth in the theory still remains to be settled. In the historical sketch which has been given I have indicated most of the arguments which the supporters and the opponents of the doctrine have adduced; these I need not again refer to, but may simply state briefly what I regard as the correct view to take of "maternal impressions." In order to centralise our knowledge on the subject, I may ask myself two questions: (1) Does a definite impression upon a pregnant woman's mind often or ever cause a defect in the fœtus closely resembling the thing producing the impression? and (2) Has the state of the mother's mind during gestation any effect upon her unborn infant's development?

The first question I answer in the negative, and the second affirmatively. Since I wrote upon the subject some years ago I have very carefully examined the evidence upon which several alleged cases have been founded, I have had opportunities of attending confinements in which all the elements regarded as suitable for the production of the results of an impression were present, and in which the children were free from anything at all resembling the impression, and I have very fully acquainted myself with the voluminous literature of the subject. The conclusion drawn is, that the cases which have been advanced to prove the potency of maternal impressions have been accidental coincidences, and not the effects of the alleged causes. Their great number may be adduced to prove that the doctrine must contain an element of truth; but it has to be pointed out that, numerous as they are, the cases in which nothing of the kind happened are vastly more numerous. Further, although I do not wish to lay too much stress upon this, no adequate scientific explanation of the *modus operandi* of such impressions has ever been advanced. Whilst I am willing to admit that the mother's nervous system is often in a peculiar state during pregnancy (Neumann, *Centrlbl. f. Gynäk.*, xix. 201, 1895), and whilst I fully recognise the possibility of the mother affecting the fœtus with a disease, and *vice versâ*, I regard it as impossible for (*e.g.*) the sight of a mutilated individual to be so transmitted mentally by the mother as to cause a fœtal amputation resulting in a similar deformity in utero. At the same time, I must concede that perhaps one case in a hundred presents phenomena which it is very difficult entirely to explain away. One such case I have myself met with; but it seemed to me reasonable enough to think that a more rational explanation of it existed, although as yet unknown, than the influence of the mother's imagination.

With regard to the second question, I think there can be no doubt that prolonged or strongly marked mental states of the mother may affect the development of the fœtus in her uterus. That such can produce abortion none, I fancy, will deny; and that short of producing miscarriage they can also lead, through vascular and nutritive disturbances, to irregularities in embryogenesis is eminently probable. In Paris, it is said, the children that were conceived during the disastrous siege of the Franco-Prussian war can be recognised by bodily and mental stigmata so marked that they have been called "enfants du siège." In reference to this phenomenon Féré (*La Famille Neuropathique*, p. 22, 1894) says "les enfants qui ont été conçus et portés à certaines époques troublées offrent en grand nombre des troubles de nutrition, des malformations et en particulier des altérations des fonctions du système nerveux." Of course it must be admitted that the poor or bad food and the defective hygiene of such seasons were also operative, still it is reasonable to believe that in part the results were due to the continued and severe terror and constant anxiety incident to a time of siege in modern warfare. In the same way the results are not always teratological, but may, as Féré has also shown (*Teratologia*, ii. 245, 1895), be of the nature of sterility, abortion, premature labour, mortinatality, congenital debility, and retarded growth and development. There are then many causes at work and many resulting phenomena; but amongst the former it is fair to reckon mental emotion, and among the latter monstrosities. To this extent I believe in the old doctrine of maternal impressions; this is, I think, the one grain of truth in an immense mass of fiction and accidental coincidence.

In order that more light may be thrown upon this matter, cases in which mental impressions in pregnancy were followed by the birth of infants *in any way abnormal* ought to be put on record. For instance, Féré recounts how a woman, pregnant four or five weeks, was greatly impressed by the sight of a child with a hare-lip; at the full time all her friends came together to see an infant born similarly affected, but the offspring showed not a hare-lip but a large nævus on the neck (" Un fait pour servir à l'histoire des bouffées de chaleur et des rougeurs morbides," *Compt. rend. Soc. de biol.*, 10 s. i. 643, 1894). It is by no means certain that this was an instance of cause and effect, but such cases are far worthier of record than are those in which an impression is said to reproduce itself, as regards form and situation, on the infant's body.

CHAPTER X

Teratogenesis (*cont.*): Theories of the Present; Traumatism and Mechanical Pressure as a Cause of Monstrosities; Extra-genital Maternal Traumatism; Injuries affecting the Mother's Abdomen; Intra-abdominal Pressure; Intra-uterine Pressure; Funic Pressure, with Literature.

WHILE, as has been shown in the preceding two chapters, some of the teratogenic theories of the past are represented by modern developments, so also some of the present views spring from notions with which the ancients were acquainted. The division, therefore, of the theories of the causes of monstrosities into past and present is artificial and somewhat inaccurate; but some sort of classification is necessary, and the one employed has the merit of being at least convenient. Thus it comes about that the last of the beliefs of the past (maternal impressions) in a certain sense still exists, while the first of the beliefs of the present (traumatism) has its roots in antiquity.

The idea that antenatal deformities might be due to causes acting mechanically upon the fœtus was present in the mind of Hippocrates when he wrote in his treatise *De Genitura* the passage which may thus be rendered: "As to the infant crippled in the womb, I say that it is crippled in consequence of a contusion, the mother having been struck on the place corresponding to the fœtus, or having had a fall, or having sustained some other form of violence. If the infant experience a contusion, it becomes crippled in the part contused; if the contusion be greater, the membrane which surrounds it ruptures, and the woman aborts. Or yet again, infants become crippled in the following way: when in the womb there is a narrowness at the part where in fact the crippling is produced, it is inevitable that the body moving in a narrow place shall be crippled in that part. It is thus that trees which in the earth have not enough space, and are hindered by a stone or other thing, become bent during growth, or rather become large in one part and small in another. The infant experiences the same thing when, in the womb, a portion is relatively too narrow for the corresponding part of the infant."

This quotation does not indeed refer to monstrosities, but only to such deformities as club-foot and congenital dislocations; but it is still of great interest, being the earliest expression of a belief in the moulding power of the uterine environment. It will be specially noted that Hippocrates referred both to the sudden and temporary action upon the fœtus as seen in a maternal traumatism, and to the gradual and more permanent effect produced by narrowness or straitness of a part of the uterus.

Aristotle went a great deal farther than the Hippocratic writers, for he suggested the manner in which true monstrosities were produced, and perceived that the cause must act during the early period of embryonic life. In the fourth book of his *Generation of Animals,* and in the third chapter, where he is writing of the eggs of birds, Aristotle makes this statement (I translate from the masterly rendering into French by Barthélemy Saint-Hilaire, *Traité de la génération des animaux d'Aristote,* ii. 277, 1887): "When the germs are very close together they fuse, as very often happens with fruits in the vegetable world. When the vitelli ('les jaunes') are separated by the membrane, two chicks are produced showing nothing abnormal; but when the vitelli are in contact and nothing isolates them, monstrous chicks are produced which, while they have only one head and one body, possess four feet and four wings, for the upper parts are formed from the white, and the nourishment coming from it (this white) has been portioned out at once to them, while the lower part has only appeared later, the nourishment being single and indivisible." The latter part of the passage is obscure, but in the first part the idea of pressure acting as a teratogenic factor in embryonic or germinal life is clearly indicated, even if not expressly stated in so many words. Further, the absence of juxtaposition of the ova is afterwards adduced to explain why double monsters are less common in serpents, and why they do not occur in bees and wasps where the ova are in separate alveoli. Monstrosities, Aristotle continued, are more common in the animals that have several young ones, and herein lies the reason why they are less often met with in the human subject. The idea of pressure acting at any rate as a secondary factor in the production of monstrosities is, therefore, at least as old as Aristotle; and it is impossible to read the passages quoted without again wondering at and admiring the extraordinary insight into the deepest mysteries of Nature which the peripatetic philosopher possessed so many centuries ago.

Aristotle's writings indicated the high-water mark of teratological knowledge, both human and comparative, for more than two thousand years; and even at the present day and with all modern methods of research, including the microscope, at our command, we have not, after all, advanced the subject very far beyond the point at which it was then left. Observations have indeed been multiplied until it has become a task of some magnitude to collect together all the recorded cases of any one kind of monstrosity, but I doubt whether we really see much farther into the very heart of the matter than did Aristotle.

In the Hippocratic and Aristotelian writings are found the roots, so to speak, of the belief in the teratogenic power of traumatism and pressure acting upon the organism yet in the womb; but more than two thousand years had to pass by before the tree blossomed out into the full growth of the modern theory of the production of malformations by mechanical influences. Paré (*Des monstres tant terrestres que* *marins*, Paris, 1573. Translation by Th. Johnson, p. 597, London, 1678), among the many causes of monstrosity which he enumerated, placed narrowness of the womb and external violence: in writing of the sixth cause he says, "We are constrained to confess by the event of things, that Monsters are bred and caused by the straitness of the Womb; for so Apples growing upon the Trees, if before they come to just ripeness they be put into strait Vessels, their growth is hindred. So some Whelps which Women take delight in, are hindred from any further growth by the littleness of the place where they are kept." Allusion is then made to the distortion of the roots of trees by a "Flint or any other solid body," and it is affirmed that since "by the opinion of Naturalists, the place is the form of the thing placed, it is necessary that those things that are shut up in straiter spaces, prohibited of free motion, should be lessened, depraved, and lamed." To continue, Paré's seventh cause is the "ill-placing" of the pregnant woman: "They which sit idlely at home at the time of their being with Child, as cross-legged, those which holding their heads down, do sew or work with the needle, or do any other labour, which press the belly too hard with cloaths, breeches, and swathes, do produce children wry-necked, stooping, crooked, and disfigured in their feet, hands, and the rest of their joints." In confirmation hereof Paré adds the illustration of an infant with crooked hands and feet so produced. The eighth cause is injury to the mother "by reason of a stroke, fall from on high, or the like occasion" through which the fœtal bones are affected or a vein opened, with the result that the infant loses nourishment and is small or altogether monstrous.

In the views of Paré will be recognised those of Hippocrates, with some picturesque amplifications but with a loss in scientific exactness. In them, as in the Hippocratic conception, the underlying theory is the action of pressure either temporary and violent, or long-continued but less severe, upon the uterine contents; the cause of the pressure may be the uterus itself, the parts surrounding the uterus, or extra-corporeal agencies. Paré's opinions are closely allied to those of Lemnius (*De miraculis occultis naturæ*, lib. i. c. viii. p. 34; lib. iv. c. vii. p. 380, Francofurti, 1628), for he enumerated (along with faults in the *materia*, the influence of the mother's imagination, and the effect of the stars) defects in the constitution of the uterus; and he compared the growth of the fœtus in utero to the casting of a metal into a particular form, when faults in the mould as well as in the material moulded would lead to deformities. M. Weinrichius (*De ortu monstrorum commentarius*, c. xiv. 127, 132, Breslæ, 1597), also, among the causes which he named, placed uterine pressure; for we read that if the uterus cannot distend suitably to accommodate the fœtus ("quod si igitur uterus in figuram fœtui convenientem dilatare se non potest") then a monstrosity results. The comparison with apples in a bottle is adduced as proof; and reference is made to the Hippocratic doctrine of the mutilating effect upon the fœtus of violence happening to the mother. In the work of Ulysses Aldrovandus (*Monstrorum historia*, p. 380, Bononiæ, 1642), prepared by Ambrosinus, the narrowness of the uterus is spoken of as one among several teratogenic causes—"ratione angustiæ receptaculi fœtus, monstra nascuntur."

F. Licetus (*De monstris*, lib. ii. c. v. p. 67; c. xvi. p. 100; c. xx. p. 108; c. xxiv. p. 121; c. xxxi., xxxii., and xxxiii. pp. 136–138; c. xxxix. p. 144; c. xli. p. 145, Patavii, 1668), writing about a hundred years after the time of Paré, dealt fully with the various ways in which pressure may act upon the fœtus; at this we need show no surprise, for he enumerated most carefully every known or suggested factor in teratogenesis. The uterus may be too narrow to allow a perfect infant or perfect twins to be formed; and the narrowness may be due to a tumour occupying part of the cavity and attached to the uterus, or to the membranes, or to the placenta; or it may be caused by an extrauterine growth; or, again, it may result from tight-lacing. Through violence affecting the mother the parts of two fœtuses may be driven together and caused to unite. The presence of a "mole" in the uterus may also have a deforming effect upon the fœtus. In view of recent discoveries it is specially noteworthy to find in the teratogenic system of Licetus a prominent place given to tightness of the membranes enveloping the fœtus.

Here is an interesting observation from the close of the seventeenth century. In 1680 united twins were born in the town of Ebeleben, and B. Scharfius (*Miscell. Acad. nat. curios.* (1683), Dec. ii. Ann. ii. obs. cii. p. 254, Norimb., 1684) unhesitatingly ascribed their production to abdominal constriction applied on the part of the mother to conceal her pregnancy. He entitled his observation "Monstrum a constrictione," and warned pregnant women against such practices lest they should, like the unfortunate of Ebeleben, bring forth monsters. L. Schröck, however, in a *Scholium* following Scharf's paper, threw grave doubts upon the explanation, and pointed out that many women illegitimately pregnant tight-laced, and yet brought forth normal infants, and that in cases like the twins of Ebeleben the history of abdominal compression was generally wanting. Further, he enforced his argument by referring to the absence of any cicatrix indicating the point of fusion, to the presence of normally formed parts in the conjoined twins, and to the want of any sign of such hæmorrhage as ought to have occurred when the two hearts violently became one (!). Schröck himself regarded the phenomenon as due to the presence of two cicatriculæ or "treads" in the ovum.

Early in the next century (the eighteenth), the doctrine of monstrosity by mechanical causes came prominently to the front in connection with the famous series of discussions in the Parisian Academy of Sciences. In 1706 Du Verney (*Mém. de l'Acad. roy. des sciences*, Ann. 1706, p. 431, Paris, 1731) described an interesting case of double monster (recognisably an instance of *dicephalus leeanopagus*, as we may call it at the present day), and stated that he did not regard such a phenomenon as the result of chance or of a blind formative power, but as the exhibition of a divine intelligence making plain the constructive resources of the Creator. Eighteen years later Lemery (*ibid.*, Ann. 1724, p. 44, Paris, 1726), also in connection with a case of joined twins (classifiable by us now as *dicephalus somatopagus*), argued against the idea of germs originally and essentially monstrous as propounded by the philosopher P. S. Régis (in 1690) and repeated by Du Verney; with considerable skill he stated the case for the pressure-theory without at all clearly indicating the kind of pressure referred to. He found an explanation of the structural peculiarities of double terata in the action of a moderate or a strong pressure acting in this or that direction. A moderate compressing force, he thought, caused the fusion of external parts, while a stronger one was needed to unite the internal organs of the two fœtuses. In Italy, also, Vallisneri (*Istoria della generazione*, p. 250, 1721) had spoken of an external compressing force in connection with absent limbs or parts.

Some years later Winslow (*Mém. de l'Acad.*, Ann. 1733, p. 366, 1735; Ann. 1734, p. 453, 1736) appeared as a supporter of Du Verney's notion of original monstrosity, and consequently as an opponent of the accidental theory of origin of Lemery. This writer discussed in order a large number of reported cases of malformation and monstrosity, pointing out that in them all there existed grave technical difficulties preventing the acceptance of a mechanical and accidental teratogenic cause. In a very special way did these difficulties exist in the cases of transposition of the viscera, double uterus, polydactyly, supernumerary ribs and vertebræ, and extraordinary arrangements of muscles. Stimulated doubtless by Winslow's criticism, Lemery (*ibid.*, Ann. 1738, pp. 260, 305, Paris, 1740; Ann. 1740, pp. 109, 210, 324, 433, 517, and 607, Paris 1742) now published a series of exhaustive memoirs on the two competitive theories of the causation of monstrosities; in these he endeavoured, *inter alia*, to discredit by theological arguments the idea of germs originally monstrous, while he supported his own opinions as to their origin from mechanical influences acting upon germs originally normal by an appeal to many anatomical peculiarities found especially in double terata. He wrote much about pressure, but did not very clearly define what he meant thereby, although in one passage at least he appears to have been referring to that produced by uterine contractions. Winslow (*ibid.*, Ann. 1740, p. 586, Paris, 1742), in connection with the description of an acephalic twin, took up the matter again, reiterated his views, and maintained that, far from depreciating the attributes of the Creator of the Universe, they rather rendered homage to His all-powerful sovereign liberty ("à sa toute-puissante liberté souveraine"). He contributed two other papers (*ibid.*, Ann. 1742, p. 91; Ann. 1743, p. 335, Paris, 1745) on the subject; and doubtless Lemery would again have replied had not death seized him and so closed in an emphatic and certain manner this long controversy.

A perusal of the various memoirs (a work, by the way, of no little magnitude, yet of intense interest to those who are concerned about such matters) makes it clear that, on the whole, Lemery had the best of the argument; for Winslow certainly resiled from certain positions originally occupied by him, and this too notwithstanding the fact that he had that highly coveted advantage, the last word. It was a memorable controversy, "une longue et solennelle discussion" Saint-Hilaire called it, and not without cause; it showed now and again a tendency to wander away from teratology into teleology, and it was not altogether free from the *odium theologicum*; and it is interesting to us now chiefly from the light that it throws upon the theory of monstrosity by pressure and traumatism as it was held in the first half of the eighteenth century. It was useful because it stimulated the gathering together and preservation of many records of individual cases of malformation; but it ended in a somewhat disappointing fashion, as indeed it could only be expected to do, the state of knowledge upon Embryology being at that time what it was. For they who took part in or listened to the discussions were hampered by their ignorance of the possibility that monstrosities might be due to accidental causes acting before impregnation or, at any rate, before the rudiments of the embryo were laid down. It was not till 1759, or sixteen years after the death of Lemery, that the idea of the pre-existence of germs, normal as well as monstrous, was discredited through the labours of Caspar F. Wolff and the establishment of the theory of epigenesis. At the same time, had Lemery and Winslow explored the writings of Harvey, and especially his *Exercitationes de Generatione Animalium*, they would have been equipped, long before Wolff's time, with the knowledge of the great law that the complex animal arises from a relatively homogeneous germ by gradual differentiation or epigenesis; to both Lemery and Winslow this knowledge would have been of no little value, and might, also, have greatly clarified some of the dark parts in their disagreements. (If my readers have doubts about Harvey's claims in these embryological matters they ought to peruse W. K. Brooks' convincing arguments as set forth in the *Johns Hopkins Hospital Bulletin* (vol. viii. p. 167) in 1897.)

While it is true that the Lemery-Winslow discussion in the French Academy of Sciences as well by its magnitude as by the personnel of the contestants dwarfed all contemporaneous writing on the pressure-theory of teratogenesis, the existence of such writings must not on that account be forgotten. The authors of these contributions took sides in the great controversy, and one of them (A. von Haller) even intervened in the debates. Haller at first supported Winslow; but some years later, when the controversy had passed from France into Germany, he admitted that there was much force in several of the arguments of Lemery, and conceded that anencephaly might arise from some external injury ("ab aliqua injuria externa"). Haller's views are to be found in several scattered papers published between 1735 and 1745; they are gathered together along with his later opinions in his treatise "De Monstris" (*Opuscula sua anatomica*, 1751). A passing reference is all that need be made to the writings of other contemporary scientists. Vallisneri (*Istoria della generazione dell' uomo e degli animali*, p. 249, Venezia, 1721), for instance, affirmed that double terata resulted from the union of the originally separate ova; E. Sandifort ("Anatome infantis cerebro destituti," p. 66, in his *Opuscula anatomica*, Lugd. Batav., 1784) ascribed fœtal anencephaly, in a case known to him, to the falling of the mother backward downstairs during her pregnancy; and Fabri (quoted by Taruffi, *Storia della teratologia*, i. 254, 1881) instanced spasmodic uterine contractions due to violent mental emotion or hysteria as possible compressing and deforming forces. There were others, however, who showed a less complete attachment to the mechanical theory of teratogenesis: Riviera (quoted by Taruffi, *op. cit.*), in describing a cyclops fœtus, opposed the pressure-theory, arguing that the regularity of the arrangement of parts and the absence of marks of compression militated against it; and S. T. Sömmerring (*Abbildungen und Beschreibungen einiger Misgeburten*, p. 35, Mainz, 1791) did not agree with Siebold in his belief that tight-lacing was a sufficient cause for fœtal encephalocele.

In the closing years of the eighteenth century there was a distinct diminution in the popularity of the pressure-theory among medical men, a change in opinion to which Morgagni in great measure contributed by his promulgation of the view that fœtal diseases (*e.g.* accumulation of fluid in the body cavities) are the direct causes of monstrosities. The nineteenth century, however, witnessed a great revival and development of the idea that antenatal mechanical action had an important influence in teratogenesis, and in its scientific form the doctrine is to-day regarded by many teratologists as adequate and satisfactory, *but*, let it be observed, *only in its scientific form.* It did not by any means gain acceptance at once, for J. F. Meckel (*Handbuch der pathologischen Anatomie*, Bd. i. pp. 21, 29, etc., Leipzig, 1812) denied the teratogenic efficacy of mechanical causes, among which he placed irregular position, the pressure of one fœtus on another, and abnormalities in the form of the uterus; he repeated many of the arguments of Winslow, instanced the cases of twins, one of which was a fœtus compressus but otherwise normal; and he pointed out that mechanical agencies afforded no explanation whatever of hereditarily transmitted structural anomalies. Other writers followed the example of Meckel; nevertheless the theory grew in importance, became more and more elaborated, and constantly added to the number of its adherents (*vide* Hans Koch's Dissertation, *Ueber die auf mechanischer Ursache beruhenden congenitalen Deformitäten*, Köln, 1895).

In order, however, that we may understand the history of this teratogenic theory in the nineteenth century, it is necessary clearly to recognise certain preliminary facts. It must, for instance, be noted that the pressure-theory as stated by one observer differed widely from that enunciated by another: there is, in one sense, all the difference in the world between the idea of tightly laced corsets causing fœtal malformations and the doctrine of the production of monstrosities by the constricting force of the umbilical cord, of bands of lymph, or of amniotic membrane. One may hold the latter theory without swearing allegiance to the former. The idea of *pressure* is present in all these hypotheses, but the kind of pressure meant and its mode of action differ widely. Again, it has to be borne in mind that while some have regarded pressure as the ultimate and only cause of teratological formations, others have rather looked upon it as one among many causes, or as the incidental circumstance which brings into play other factors, such as intrauterine inflammations, arrested developments, and the like. For these and for other reasons it will be necessary to consider the various pressure-theories separately, each one on its own merits. For this purpose I have attempted to classify them provisionally into two primary groups, according as the pressure is supposed to act upon the fœtus from without or from the inside of the mother's abdomen. In each group there are two or three sub-groups, corresponding to the exact nature and sphere of action of the pressure in operation. Thus, in the first group are placed injuries to the mother's body in its various parts, the continuous pressure exerted by tightly laced stays, and blows upon or wounds of the abdomen; while in the third group are found the constricting pressure of the umbilical cord, etc., the compression of one fœtus by another fœtus or by one of its own limbs, and tightness of the amniotic membrane. Here is the arrangement in a tabular form.

Pressure[1]-Theories in Teratogenesis.

I. External Pressure—
  (*a*) General Maternal Traumatism, *e.g.* falls and blows.
  (*b*) Injuries to and Pressure affecting the Maternal Abdomen, *e.g.* corsets.

II. Internal Pressure—
  (*a*) Intra-abdominal and Intra-pelvic.
    1. Abdominal and Pelvic Tumours.
    2. Pelvic Contraction.
    3. Narrowness and Malformation of the Uterus.
  (*b*) Intrauterine—
    1. Uterine Tumours.
    2. Twin Fœtus.
    3. Fœtal Limb.
    4. Umbilical Cord.
    5. Amniotic Bands and Amnion.

Some space may be devoted to each of these variants upon the pressure-theory in teratogenesis.

Maternal Traumatism (Extra-genital).

The first of the pressure-theories which I shall describe regards it as possible that a maternal traumatism, a blow or other injury, occurring outside the genital sphere, may produce a monstrosity or at least a malformation. For instance, in the year 1895, I was examining a child, three years of age, who had a congenital contracture of the index finger of both hands and talipes calcaneus of the left foot; the mother at once volunteered as an explanation of her child's deformities the information that three weeks before labour (which occurred at the seventh month) she had fallen downstairs. Again, some years ago, a medical man sent to me for dissection an anencephalic fœtus, and stated that the mother had knocked her head against a gas bracket during the early part of her pregnancy; he wished to know if there could be any connection between the maternal traumatism and the condition of the fœtal head.

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[1] It is to be observed that the word "pressure" is used in the wide sense which includes the notion of transient but excessive pressure as seen in a blow or fall.

Reports, such as the two cited above, are far from uncommon in medical literature, but the medical man does not always or indeed often accept the explanation advanced by the mother of the malformed infant. He commonly records the statement without expressing an opinion as to its worth. Let me here briefly allude to some of these alleged teratogenic causal conditions.

In the first place, several such statements are to be found in the *Transactions of the Edinburgh Obstetrical Society*. In 1852, in connection with Fenton of Alyth's case of anencephalus (*Edinb. Month. J. Med. Sc.*, xv. 170, 1852), it was noted that in early pregnancy the mother had strained herself in lifting a box; in 1882, A. R. Simpson in a Maternity Hospital Report (*Trans. Edinb. Obst. Soc.*, vii. 115, 1882) referred to an instance, also of anencephaly, in which there was much lifting of heavy weights in pregnancy; and in a paper which I myself communicated in 1892 (*Trans. Edinb. Obst. Soc.*, xvii. 99, 1892) were recorded cases in which a sprain of the mother's ankle was the alleged cause of talipes varus in the infant, in which a dog bite on the mother's leg was looked to as the origin of a scar on the leg of the fœtus, and in which a blow on the mother's chest was followed by the birth of a child with a nævoid patch in the corresponding region.

Some cases from other sources may also be noted to illustrate different types of this belief. J. S. Beale (*Lancet*, ii. for 1863, p. 27) saw an infant born with a black eye whose mother had been struck over the eye eight hours previous to her confinement. G. E. Jeaffreson (*Lancet*, ii. for 1866, p. 568) met with an example of anencephaly in which the mother at the second month of her pregnancy had suffered from a severe injury to the head. E. A. Martin (*Ueber Selbstamputation beim Fötus*, Jena, 1850) recorded the birth of a child whose left arm was represented by a short stump and whose mother had had a fall in pregnancy; the separated part of the limb was expelled with the placenta. F. Ormrod (*Lancet*, i. for 1875, p. 393) gave the history of a pregnancy in which the mother had the fingers of her right hand crushed in a door and her child showed defective development of the fingers of the right hand. At a meeting of the Royal Academy of Medicine in Ireland (November 25, 1882) M'Ardle described a case of spina bifida and other malformations in a fœtus, ascribed to the fact that the mother when three months pregnant had been in a railway accident and had got her back injured.

Such records might be multiplied, but with this small fasciculus of illustrative instances the reader may well be satisfied. If he will scrutinise them it will soon be apparent to him that here after all we have no new theory of teratogenesis but only an old one masquerading in a new garb; it is simply the doctrine of maternal impressions in a slightly veiled form. The impression, it is true, is physical as well as mental, but the idea of its *modus operandi* is much the same; the scientific mind finds it scarcely less difficult to accept the notion of a physical than of a purely mental influence. Nevertheless, the theory is of interest, for it serves as a link joining together the theories of the past with those of the present. Save for this purpose it might be safely allowed to pass into the oblivion of the immemorabilia of our subject.

At the same time there is one sense in which traumatism outside the genital sphere may possibly be potent for the production of deformity. If it be accepted that falls and blows may by a process of *contre-coup* lead to the occurrence of fœtal fractures, wounds, and dislocations, then it may also be believed that the injured parts may during healing become distorted and even malformed. Dieterich (*Med. Cor.-Bl. d. württemb. ärztl. Ver.*, Stuttgart, viii. 5, 1838), at any rate, reports a case in which a fall by the mother upon her back was apparently the cause of wounds of the fœtal head and fracture of the forearm. It would seem that this result would be more likely to follow if there were little or no liquor amnii in utero, although in Dieterich's case the membranes were unruptured at the time of the accident. The effect of fœtal fractures in the production of malformations falls, however, more naturally to be considered with the next theory, that, namely, which regards pressure applied directly to the maternal abdomen as a teratogenic agency.

What Morgagni, writing in the eighteenth century, thought about the theory of traumatism outside the genital sphere may be gathered from the following extract from his great work (*De Sedibus et Causis Morborum*). I quote from Alexander's translation (vol. i. p. 272, Letter xii. article 16, London, 1769). Morgagni is speaking of a child with spina bifida. "But to return to our boy: not being ignorant of the excessive credulity of other people, at some times, I ask'd, however, from the mother, whether, as she was in the flower of her life, and both she and her husband healthy, she had ever fall'n on her back, while she was pregnant with this child, which was her first-born, or had received a blow in that part by any means, or had dreaded, or been frighten'd at any thing; or, in fine, whether she had long'd for any thing: all which she immediately and expressly answer'd in the negative; although afterwards, as the custom is with these weak women, it came into her mind, that she had wish'd for a fig." Morgagni, it is evident, was no believer in impressions, mental or physical.

Injuries affecting the Mother's Abdomen.

A less incredible theory than that just considered is founded upon the action of external pressure upon the mother's abdomen during pregnancy. Such pressure, it may be reasonably supposed, bearing as it does more directly upon the organ which contains the young fœtus, will be more likely to have injurious effects upon it than injuries to the head or limbs of the mother. The abdominal pressure may be long-continued and not excessive, or it may be short, sharp, and severe.

The practice of tight-lacing for the concealment of pregnancy suggests itself as a form of abdominal compression likely to have teratogenic effects. It appealed, as we have seen, very strongly to Scharfius (*loc. cit.*), and in the nineteenth century also it had its advocates. Etienne Geoffroy Saint-Hilaire ("Sur un fœtus né a terme, blessé dans le troisième mois de son age, et devenu monstrueux à la suite d'une tentative d'avortement," *Mém. Soc. méd. d'émulat. de Paris*, ix. 65, 1826) described very graphically the case of "Julie," who, finding herself pregnant, and desiring to conceal the fact from her sister with whom she lived, endeavoured to bring her pregnancy to an end by wearing very tight corsets. "Elle se compose un corset lardé de buscs épais ; elle se plastrone le ventre de manière à placer au dehors une force vive, réagissante et destructive des développemens intérieurs." Nevertheless she arrived at the full term and gave birth to an infant with a monstrosity of the head, to which Saint-Hilaire gave the name *thlipsencéphale* ("cerveau écrasé"). Isidore Geoffroy Saint-Hilaire (*Histoire des Anomalies*, iii. 534, Paris, 1836) evidently accepted his father's views concerning the teratogenic power of tightly laced stays ; but he dwelt more upon the effects of blows and falls upon the abdomen, and to this subject I shall refer immediately. Hohl (*Die Geburten missgestalteter, kranker und todter Kinder*, p. 102, Halle, 1850) had much difficulty in finding arguments in support of the maleficent effect of the corset : he reported a case of tight-lacing in which the fœtus was born with deformed extremities ; but there was also hypospadias, and he was puzzled to account for the latter malformation on the corset hypothesis.

It is somewhat striking that the pathologists and teratologists who followed the Saint-Hilaires do not seem to have been specially impressed with the idea of corset-pressure in teratogenesis. Bouvier (*Bull. Acad. de méd.*, Paris, xviii. 355, 389, 1852–53 ; *ibid.*, xx. 1106, 1854–55 ; *Dict. encyclop. d. sc. méd.*, Paris, xx. 745, 1877), for instance, in his several articles upon the medical aspects of the corset, refers to its effects in producing abortion and causing imperfect development of the fœtus, but he gives no details of cases, and indeed states that he had watched three instances of tight-lacing in pregnant women, and in all of them there were no ill consequences at all. It is also a striking fact that the writers who have so emphatically condemned the corset as "the evil of the age," and the active cause of pelvic congestion, of defective secretion of bile, of dyspepsia and the like, have little or nothing to say of its teratogenic influence upon the unborn infant. One is driven to the conclusion that its ill effects, in this direction at least, are few; perhaps the presence of the liquor amnii is the great safeguard of the fœtus.

There is, however, another form of abdominal pressure which must be referred to; I mean that produced by falls or blows, by direct contusion or by *contre-coup*. Several kinds of malformation and monstrosity have been freely ascribed to injuries affecting the mother's abdomen in the early months of pregnancy, and many instances from medical literature might be cited as proof. Let me here simply present a small fasciculus of illustrative cases; it will suffice. Roux (in Breschet's article, *Arch. gén. de méd.*, xxvi. 38, 1831) described a case of occipital encephalocele in an infant whose mother had fallen downstairs at the seventh month of pregnancy; Rayer (*Compt. rend. Soc. de biol.*, 2 s., ii. 103, 1856) reported how a mulatto woman at the sixth week of pregnancy had been ill treated by her husband and had given birth to an anencephalic fœtus whose malformed head was adherent to the amnion covering the placenta; C. C. Werthheim (*Monatsschr. f. Geburtsk.*, ix. 127, 1857) met with a case of twins, one of which had died early in pregnancy, while the other showed a large spina bifida with absence of the sacral and coccygeal vertebræ, and the mother had received a severe kick in the left inguinal region from her husband some weeks before the mid-term of her gestation; instances of exstrophy of the bladder following upon a fall and a blow by a cow's horn on the abdomen respectively were reported by A. Freund (*Arch. f. Gynaek.*, iii. 381, 1872) and James Mowat (*Med. Essays and Observ. Soc. in Edinburgh*, iii. 276, 1735); an example of anterior encephalocele was attributed by R. Hein (*Ztschr. f. Geburtsh.*, vi. 352, 1881) to a jump which the mother made from a carriage when she was three weeks pregnant; and W. Graeffner (*Deutsche Arch. f. klin. Med.*, xxxiii. 95, 1883) related how a woman, a few days before her confinement, fell on a rock, and her infant was born with a deformity of the sternum (sternal cyphosis or *Trichterbrust*). Histories somewhat similar to these given above were related by T. G. A. Roose (*Diss. inaug.*, Gottingæ, 1793), by P. Vannoni (*Gazz. med. ital. feder. Tosc.*, 2 s., i. 394, 1850), and by O. Werler (*Diss. inaug.*, Berlin, 1881). The Saint-Hilaires, father and son, expanded this theory of abdominal traumatism, and endeavoured to give to it a degree of scientific exactness. They maintained (*Histoire des Anomalies*, iii. p. 534, 1836) that two varieties of deformity of the head (nosencephaly and thlipsencephaly) resulted from it, and that when the violence occurred at the fourth month the former would follow, while if it took place at the third month the latter monstrosity would be developed; the earlier in pregnancy the traumatism took place the further removed from the normal would the infant be. Vrolik (Todd's *Cyclopædia of Anatomy*, iv. 943, 1849–52), also, and Förster (*Missbildungen des Menschen*, p. 5, Jena, 1865) have admitted the possibility of the teratogenic potency of injuries to the mother's abdomen in pregnancy. In a case published by Kriwsky (*Monatschr. f. Geburtsh. u. Gynaek.*,

vi. 895, 1900) the mother of an infant with exomphalos and deformed limbs had to spend twelve hours daily in a squatting posture at her work.

It must, I think, be admitted that abdominal pressure and traumatism have some influence in the production of monstrosities and malformations; at the same time I do not regard it as great. What I have said in the first part of this MANUAL (pp. 177, 393) regarding fœtal fractures, dislocations, and wounds, and their origin from external violence, may, I believe, be repeated concerning the genesis of monstrosities. There is good evidence that traumatism in early pregnancy is sometimes followed by the birth of an abnormal infant, just as there is good evidence that blows and falls in later pregnancy may be followed by the birth of a fœtus showing fractures or dislocations, or both,—E. Gurlt's article (*Monatsschr. f. Geburtsk.*, ix. 321, 401, 1857) with its long list of literature is sufficient to demonstrate this,—but in many cases no such history of injury is forthcoming, and in many others there is a record of injury but no development of morbid results. Doubtless the amount of the liquor amnii present in the uterus, the existence of abnormal fragility or abnormal resistance of the fœtal bones and tissues, the relaxed or contracted condition of the abdominal muscles at the time of the injury, and many other modifying or determining circumstances have an effect upon the result, and ought, if we had knowledge of them, to be taken into account. It has to be borne in mind, also, that when we have admitted the teratogenic power of abdominal traumatism we have by no manner of means defined or explained its mode of action. Does it act directly upon the embryo, crushing or wounding it in any part, with the result that the malformed part is the immediate consequence thereof, modified and masked by the subsequent growth of that part and of the surrounding structures? Does it not rather cause a morbid state of the uterine walls, placenta, or amnion, which in process of time reacts upon the developing embryo or fœtus? Both are possible, but the latter seems the more probable.

Intra-abdominal Pressure.

Intra-abdominal pressure may conceivably act upon the fœtus in utero, and it may be of two kinds. It may consist in a compression of the whole uterus in virtue of a pelvic contraction (due to deformity of the pelvis or to neoplasms inside it) or of an abdominal tumour, or it may be a purely uterine pressure caused by narrowness or by malformation of the uterus itself. We have little or no evidence that pelvic contractions or abdominal and pelvic tumours tend to produce malformations of the fœtus in utero (P. Vannoni, *loc. cit.*), although there are some indications that these morbid states may lead to fractures of some of the bones of the unborn infant (J. Vilcoq, "Fractures Intra-utérines," *Thèse*, p. 19, Paris, 1888), and so perhaps to deformities resulting therefrom (*e.g.* amputations, *vide* J. Y. Simpson, *Dublin J. Med. and Chem. Sc.*, x. 239, 1836). Jules Platon (*Marseille méd.*, xxxiv. 785, 1897), however, seems to ascribe pseudencephaly to the pressure of two uterine fibroids, but the evidence is not convincing.

That uterine narrowness may be the cause of fœtal anomalies is a firmly established belief; and the narrowness may be the result of contractions of the uterine muscle, or it may represent a real diminution of the size of the cavity of the womb from the presence of a malformation, such as is seen in the uterus duplex or the uterus septus. Here, again, in the first of these suppositions, the teratologist finds himself in the presence of that almost ubiquitous theory of the maternal imagination, for those who desired to give a scientific aspect to the "impression" doctrine did so by suggesting that the perturbation of the mother's mind translated itself into powerful contractions of the mother's uterus, and that these caused a temporary narrowness of the uterine cavity, with teratogenic results. But, apart from the "maternal impression" theory, many writers hold that persistent or oft-recurring contractions of the uterus in pregnancy have malforming effects upon the fœtus. O. Hourlier ("Mort du fœtus," *Thèse*, Paris, p. 45, 1880), for instance, believed that they might be the cause of fœtal deformities, dislocations, curvatures, and fractures; and many others have looked to them as the determining factors in the production of club-foot and other anomalies of the extremities (L. H. Ormsby, *Deformities of the Human Body*, p. 22, 1875; R. W. Parker and S. G. Shattock, *Trans. Path. Soc. Lond.*, xxxv. 423, 1884; H. W. Berg, *Arch. Med.*, viii. 226, 1882, and *Med. Rec.*, xxxii. 509, 1887; A. Schanz, *Ztschr. f. orthopäd. Chir.*, v. 9, 1897; and others whose names are in the Text-Books of Surgery and Orthopædics and in Literature Lists). Some of these writers (*e.g.* Parker and Shattock) are not, it is true, at all explicit as to the meaning of the term "uterine pressure" which they use so freely; but it may be inferred that pressure due to a diminution in the amount of space inside the uterus from contractions of its muscular walls has been most prominent in their thoughts. It is supposed that the special variety of club-foot produced may be explained by the date in antenatal life when the pressure became a constraining force; the foot is fixed in the position then natural to it, and the pressure being maintained, the attitude becomes permanent; and thus talipes varus is due to an earlier compression than is talipes calcaneus. Opitz (*Ztschr. f. Geburtsh. u. Gynäk.*, xl. 520, 1899), also, has described a case of hyperextension of the knee in a fœtus which was the offspring of a woman with a uterus duplex, and has traced back the deformity to narrowness of the pregnant side of the uterine cavity; E. Zuckerkandl (*Allg. Wien. med. Ztg.*, xxiii. 247, 1878) attributed the small size of the head, the condition of the brain, and the deformed state of the feet of a fœtus to uterine pressure compressing the head against the chest; P. L. Gardini (*Ann. di ostet. e ginec.*, xxi. 705, 1899) has recorded a case of pregnancy in a bilocular uterus in which the fœtus was anencephalic, but without suggesting any relation of cause and effect between the two states; and F. Winckel (*München. med. Wchnschr.*, xliii. p. 390, 1896) has very clearly stated his belief that a narrow uterine horn (in a case of uterus bicornis bicollis) was the cause of double pes varus in the fœtus.

There are, however, not a few difficulties in the way of a full acceptance of the theory of the effect of uterine pressure in the production of even the minor malformations. E. J. Chance (*Bodily Deformities*, p. 139, 1862), under the chapter-heading "Can Position in utero produce Deformity?" referred to many of these difficulties, and dwelt specially upon the admitted coexistence of deformities and excess of liquor amnii as being a very strong argument against the pressure-theory; while Keller (*Arch. f. Gynaek.*, lxvii. 477, 1902), among recent authors, has been compelled to recognise the serious problem raised by the occurrence of hydramnios in association with monstrosities. It is practically inconceivable that the pressure of the uterine walls can have a deforming effect upon a fœtus surrounded by an excess of liquor amnii. Further, the same deformities have been met with in cases of oligohydramnion (*vide* the first section of this MANUAL, p. 407) as in those of hydramnios. Of course, it may be argued that the state of scarcity of liquor amnii preceded that of excess, and that the fœtal deformities were produced by uterine contractions in action during the former condition; but there is no actual proof of this, although E. Porro's case (*Gazz. med. di Lombard.*, s. 6, vi. 393, 1873), in which the mother's abdomen was first too small and later too large, and in which there were malformed twins, might seem to lend some support thereto.

It is doubtful whether the authors who have written with such facile pens concerning uterine pressure, and its effects on the uterine contents, have seriously considered the problem in biological physics thereby raised. The conception present in their minds seems to have been that of a rigid case with easily moulded contents; but, as a matter of fact, the uterus is not a rigid case but an organ which adapts itself both to its external surroundings and to the organism within it. Frozen sections have shown it moulded to the vertebral column, and clinical observations have demonstrated how it changes in shape with changes in the presentation of the fœtus (*e.g.* in shoulder cases). The presence of the liquor amnii also introduces a factor into the problem which increases its complexity, and appears greatly to weaken the theory of uterine pressure in teratogenesis; for the existence of this intrauterine fluid cannot but lead to the equable diffusion of pressure, and so, it would seem, to the prevention of localised deformities. For my own part, I believe that there is some truth in the theory, more especially in regard to the minor malformations which may arise during the fœtal period of antenatal life. I have met with a case of genu recurvatum in a female infant, the child of a woman who in her previous pregnancy had a miscarriage, followed by a pelvic abscess and consequent adhesions and cicatrisations; and I think it possible that in this instance the uterus was impeded in its proper gestational expansion and the contents compressed. But I do not nail this theory to the mast, for while I believe that there may be some morsel of truth in it, I am inclined rather to consider that as a rule the uterine walls, even when contracted, protect the fœtus from malforming influences. Thus, in a case which I reported some years ago (*Trans. Edinb. Obst. Soc.*, xvii. 242, 1892), a fœtus was found partly expelled into the peritoneal cavity through the rent in a ruptured tubal gestation sac, and it showed multiple deformities (anchylosis of joints, etc.), which I regarded as due to the adhesions which had formed between it and the intestines of the mother. Actual adhesions between the intestines and an extrauterine fœtus are shown by Vrolik (*Tab. ad illustr. Embryogen.*, Pl. xvi., Amsterdam, 1849), in a plate taken from Cruveilhier's *Anatomie pathologique du corps humain.* H. M. Lufkin (*Amer. Journ. Obst.*, xli. 289, 1900) also has recorded a case in which a fœtus from a tubal pregnancy seems to have lain and grown for six months free in the mother's peritoneal cavity; it showed malformations of the feet, hands, and head, which were looked upon as due to "the pressure of the bony and soft structures of the mother upon the unprotected babe."

Since I have referred to cases of tubal pregnancy, it may be interesting to keep in mind that apparently the fœtuses from such ectopic gestations are not infrequently malformed. J. C. Webster (*Ectopic Pregnancy*, p. 112, 1895) states that various malformations may be found, and particularises club-foot, dislocation of limbs, exomphalos, and encephalocele; he also noted instances of flattening of the head, of compression of the face, and of amniotic bands extending from the fœtus to the sac wall. F. von Winckel, in a beautifully illustrated monograph (*Über die Missbildungen von ektopisch entwickelten Früchten und deren Ursachen*, Wiesbaden, 1902), has given details of eighty-seven cases, thirteen of which were seen by himself, in which the fœtus in tubal pregnancy exhibited malformations. Cragin (*Amer. Journ. Obst.*, xli. 740, 1900), in an article on the question whether a viable ectopic fœtus is worth saving, gives notes of a case in which the infant had a small umbilical hernia, asymmetry of the head, and a dislocation of the left hip; there was very little liquor amnii in the sac. It may, perhaps, be concluded that the walls of an ectopic gestation sac are more likely to exercise injurious pressure on the fœtus than are the uterine parietes. On the other hand, it may be that the cases in which the fœtus has shown malformations have been those in which rupture of the sac had occurred, and the infant passed into the abdominal cavity, where it would be more subject to compression by the maternal structures. In support of this opinion I note that J. W. Taylor (*Extra-Uterine Pregnancy*, p. 81, 1899) states that "malformations are most commonly met with in children of abdominal or ventral pregnancies." After all, therefore, we return to the general conclusion that the teratogenic effects of the pressure, either of the uterine walls or of those of an extrauterine sac, are not clearly proven.

Intrauterine Pressure.

It is conceivable that the fœtus may be acted upon by various structures lying inside the uterus, and that the result of such action may be the production of malformations or monstrosities. For instance, it has been supposed that *tumours, e.g.* polypi, might have such a teratogenic effect. C. Taruffi (*Storia della Teratologia*, i. 257, 1881) refers to a case published by C. M. Billard, in which a woman suffering from a uterine polypus gave birth to an infant with a cerebral hernia; the pressure exercised by the polypus was supposed to have been the cause of the localised destruction of the scalp, and of the defect in the left temporal bone which permitted the hernia. On turning to Billard's work (*Traité des maladies des enfans*, pp. 51 and 346, Bruxelles, 1835) I found, however, that there was no evidence of the existence of a uterine polypus in the case referred to (that of "Marianne Masse," obs. 79), and that it was merely a supposition of the writer that such a condition had been present. Further, Billard added, as an alternative supposition, that the pelvis may have been deformed, and that the growth of the uterus may thus have been hindered. It does not seem to me, from a study of the literature of the subject of fibroids in pregnancy, and from a personal acquaintance with six cases in which this complication existed, that there is proof that the fœtus becomes malformed from the pressure exerted upon it by the neoplasm. This form of intrauterine pressure may, I consider, be neglected as a factor in teratogenesis.

It is well known that in *twin births* one of the fœtuses is not uncommonly malformed, and the idea that his malformations have been caused by the pressure of his companion in utero has commended itself to some writers (*e.g.* Osiander and Zacchias, as cited by A. Klautsch in his Inaugural Dissertation (*Ueber ungleich entwickelte Zwillinge*, Halle a. S., 1892), and A. Förster in his *Die Missbildungen des Menschen*, p. 5, 1865). In the first part of this Manual (p. 424) I have referred to the *fœtus compressus*, by which is commonly understood a twin that has died between the third and fifth months of intrauterine existence, and has been flattened out and mummified by the pressure exercised on it by the living and growing co-twin. No one doubts that in these cases the flattening of the dead twin is produced by the compression to which it is subjected by the living one, although it is possible that the flattening may have preceded the death and been in some measure the cause of it,—possible, but not probable. It is not doubted, I repeat, that the flattening is due to pressure; but the question arises at once, Is the fœtus compressus *teratological*? If it be not a teratological phenomenon, then its value in connection with the pressure-theory in teratogenesis is largely lost. If, in other words, it be not an instance of disordered embryology, but merely a peculiarity in the pathology of fœtal death, then, from our present standpoint, it proves little or nothing. Now, Ahlfeld (*Die Missbildungen des Menschen*, p. 34, 1880) evidently regarded the fœtus papyraceus (s. compressus) as teratological, and indeed placed it in a special group among the double terata, and Schatz (*Arch. f. Gynaek.*, xxx. 367, 1887) has very fully described the manner of its teratogenesis; but a careful scrutiny of the facts seems to me to show that it is the cause of the death of the fœtus that is teratological, while the flattening is the result of pressure brought to bear upon the dead fœtus. The cause of the fœtal death would appear to be, in some instances at least, the asymmetry of the placental circulations of the twins, an asymmetry which is to the detriment of the one twin and to the advantage of the other. Of course this can only be the case in uniovular (monochorionic) twins with a common placenta and an anastomosis between the two circulations. Now, as a matter of fact, the fœtus papyraceus may be one of binovular (dichorionic) twins (as in the three cases reported by me, 159, 180, 190), and then this teratological mode of causation cannot be accepted. Under these circumstances we must look for the cause of fœtal death in compression or torsion of the umbilical cord or in placental hæmorrhages, conditions which can hardly be called teratological. We come, therefore, to the conclusion that in some cases neither the flattened state of the twin fœtus, nor the cause that led to the death that preceded the flattening, is teratological in the true sense of the word.

More light, however, has been thrown upon this subject by the discovery of true compressed embryos (*embryones papyracei*, or, to use a more classical form, *embrya papyracea*). Until recent years the compressed product of gestation had always been a fœtus, *i.e.* had had an intrauterine age of more than two months; but lately Sundberg (*Upsala Läkaref. Forhandl.*, n. F. iii. 560, 1897–98) has described a papyraceous embryo measuring only 29 mm. in length, and A. Loennberg (*Monatsschr. f. Geburtsh. u. Gynaek.*, xvi. 25, 1902) has recorded a true embryon papyraceum, for in addition to being flattened in characteristic fashion it also exhibited some branchial clefts and had only bud-like limbs. It is evident, therefore, that as early as the embryonic period of antenatal life the pressure of one twin may cause flattening of the other. Now, it is in the embryonic epoch that monstrosities arise, and we are therefore led to inquire whether there is any evidence that this geminous pressure might directly lead to their production. The fact that Sundberg's papyraceous embryo (*loc. cit.*) was also an amorphous acardiac embryo seems to support this conclusion, although, of course, it is open for us to believe that the acardiac condition was primary and led to the early death of the embryo and so to its flattening. On the other hand, there is evidence that the living (and compressing) twin may be the monstrous one, the compressed co-twin being normal save for the flattening; for Curatulo (*Ann. di ostet. e ginec.*, xvii. 287, 1895) has reported the birth of an anencephalic fœtus along with a fœtus papyraceus. There is not, therefore, sufficient evidence to enable us to decide whether or not the pressure of one twin may be the cause of teratological phenomena in the other; but a very evident necessity exists for the recognition and examination of all small papyraceous fœtuses and embryos, since these are no doubt often overlooked or regarded simply as little blood-clots or minute succenturiate placentæ.

I am inclined to think that the mechanical pressure of one twin upon the other is not a cause of true teratological developments. I do not doubt that the one twin has an influence upon the other which may lead to the production of malformations in it, but I do not recognise pressure as the *modus operandi.* I think rather that Ahlfeld (*op. cit.*), Schatz (*loc. cit.*), and others have put the clue in our hands when they ascribe the teratological effects to the vascular relations existing between the twins in their common placenta. Of this I shall write more in detail later. At the same time, it is possible, especially if the liquor amnii be in small amount, that one twin may so press upon, encumber, and embarrass the other that it exhibits at birth the indications of compression in such deformities as unilateral atrophies, depressed areas of the body, club-feet, scoliosis (E. Perdu, *La Scoliose*, p. 18, Paris, 1902), and the like. These deformities, it is to be noted, may quite well originate in the fœtal period of antenatal life (p. 6), and are not, therefore, so distinctively teratological as are those which arise in the embryonic epoch.

To summarise this somewhat extended argument: there is evidence that a dead twin in utero may have its form altered by the pressure of the surviving co-twin and be converted into a fœtus compressus; it would seem that this may occur also in the embryonic period of antenatal life and lead to the production of an embryon papyraceum; there is some support for the view that in the fœtal period one twin may cause surface-alterations (*e.g.* depressions and dislocations of parts) in its co-twin, even if the latter be still alive; but, finally, there is little or no proof that simple mechanical pressure between twins in the embryonic epoch is effective in the development of teratological states. There is a pressure between twins which has teratological results, but it is the pressure of competition for the best or largest part of the placental circulation, and so scarcely falls within the scope of our present argument.

Another form of intrauterine pressure which may possibly have deforming effects is that exerted by *the parts of the embryo or fœtus upon each other.* Like the other varieties of the pressure-theory in teratogenesis, this contains an element of truth combined with a large amount of speculation; the *data* are few, but the *quæsita* are many. It has also been pushed to absurd lengths, as when it was suggested by Jourdain (*Journ. de méd., chir., pharm.*, xxxix. 163, 1773) that hare-lip might be caused by the fœtus lacerating its upper lip with its nails, and when it was thought that cleft palate might be due to intrauterine thumb-sucking (Wynn Williams, *Lancet*, ii. for 1862, p. 619) or to the pressure of the tip of the infant's tongue. J. Jackson Clarke (*Physician and Surgeon*, i. 980, 1900) also has suggested that, in a case of club-hand, macrostoma, and pre-auricular appendages, the pressure of the hand upon the face of the fœtus had led to the deformities which were present; and Schenk (*Prag. med. Wchnschr.*, xxv. 6, 1900) thought that a congenital lateral ventral hernia was due to strong pressure of the flexed knee against the loin. A less violent hypothesis is found in the assertion that the heel of the fœtus (in the intrauterine and antenatal attitude of flexion) may cause a depression in the sternum. N. Hagmann (*Jahrb. f. Kinderhlk.*, n. F. xv. 455, 1880), for instance, reported a case in which a new-born infant showed such a condition of sternal cyphosis; the mother noticed when she was washing the child that the bath water collected (to the extent of a few teaspoonfuls) in a little depression on the anterior aspect of the chest; and the writer hazarded the supposition that the hollow in the breast-bone was due to the pressure of the heel ("Druck der Fersen auf das Brustbein"). The potency of calcaneal pressure, however, is doubted by many, including Taruffi (*Storia della Teratologia*, vii. 181, 1894) and G. D'Ajutolo (*Della Cifosi e della Lordosi sternale*, Bologna, 1898), and there are, of course, other possible explanations of these sternal defects. In fact the imbutiform or funnel-shaped thorax (*Trichterbrust* of the Germans) has been ascribed to the pressure of the chin of the fœtus in an attitude of marked flexion (Zuckerkandl, *Wien. med. Blätt.*, iii., No. 50, 1880; H. Ribbert, *Deutsche med. Wchnschr.*, x. 533, 1888), as well as to retraction of the diaphragm, rickets, heredity, external violence, and defective development of the sternum (A. Grünenthal, *Diss. inaug.*, Berlin, 1888).

There is a large amount of evidence in favour of the view that some malformations of the chest-wall may be due to the pressure of the arm of the fœtus in antenatal life. These malformations are generally unilateral, and consist in the defective development of some of the ribs and costal cartilages, in the absence of the pectorals and adjacent muscles, in the dwarfing or complete absence of the mammary gland and nipple, and in the want of the normal subcutaneous fat and hair of the affected region; the hand and arm of the affected side may also show malformations. Froriep (*Neue Notizen aus dem Gebiete*, etc., x. 9, 1839) put on record the case of a woman with absence of the right breast and defective development of the pectoral muscles and the ribs of the same side, and expressed the opinion that in the early stages of her antenatal life the right arm had been pressed against the chest-wall and had so prevented the growth of the underlying parts. G. Ritter (*Jahrb. f. Kinderhlk.*, n. F. xi. 334, 1877; *Oesterr. Jahrb. f. Pädiat.*, vii. 101, 1876) also described a new-born infant the left side of whose chest was very defective; the upper limb of the same side was poorly developed and ended in a single finger; and it was thought that the malformed state of both these parts was due to the pressure which they had exercised on each other. John Thomson (*Teratologia*, ii. 1, 1895) reported three instances of congenital thoracic deformity in which the pectoral muscles, the mamma, and one or more ribs were defective; and gathered together from medical journals and books eighty-six somewhat similar cases. In eleven of these eighty-six cases the hand of the affected side was more or less malformed, and in a few instances the forearm also was abnormal; the malformation of the hand was usually of the nature of webbing of the fingers (syndactylism). In one of Greif's cases (*Inaug. Diss.*, p. 25, Greifswald, 1891) the hand of the side corresponding to the thoracic defect (left) was smaller and more slender than the other. Thomson constructed two plates representing in diagrammatic fashion the thoracic and manual deformities in some of the recorded cases, and showing very suggestively that the level and area of the chest defect was such that part of the upper limb of the fœtus might quite possibly have lain over it. He pointed out that the defect did not correspond to anything in the normal course of development, and could not, therefore, be regarded as an arrest of the same nature as mesial fissure of the thorax and abdomen. Not only the muscles but nearly all the structures in the lower pectoral region were prone to be affected; and they were affected in a manner having no relation at all to their vascular or nervous supply. Thomson was led, therefore, to the conclusion that the fœtus was so acted on in utero that its arm was kept for a long time pressed firmly against its side, and that in consequence of this continued pressure not only was the growth of the parts retarded but the absorption of some of them was brought about. From this statement we may conclude that Thomson did not agree with some other writers in regarding the pressure of the arm as in itself sufficient to account for the results, but looked for a cause outside the fœtus which would press the arm against the side. He did not think that amniotic bands could be invoked in this case, but his reasons for holding this view are hardly sufficient. Apert (*France méd.*, xlvi. 326, 1899), in connection with a case of bilateral depression in the chest-wall with a congenital cardiac anomaly, advanced the pressure of the elbows of the fœtus as a possible cause, and in order to explain their compressing effects suggested deficiency of the liquor amnii.

Before I pass from the consideration of this particular variety of intrauterine pressure, I must refer briefly to the curious cases reported by Strassmann (*Arch. f. Gynack.*, xlvii. 463, 1894), in which the penis of the fœtus was caught and compressed between two of the toes of one of the feet. The fœtuses were otherwise malformed, exhibiting pes varus, polydactyly, cystic kidneys, etc.; and in one of them the penis, evidently on account of the pressure brought to bear on it by the toes, was in a state of paraphimosis. In F. von Winckel's case of congenital hypertrophy of the penis, this curious cause does not seem to have been present (*München. med. Wchnschr.*, xliii. 428, 1896), although the fœtus resembled in many ways that described by Strassmann. I may refer here in passing to the cases recorded by Lannelongue in which hare-lip and cleft palate are ascribed to the pressure of tumours of the jaws and tongue.

From a survey of the facts that have been narrated in the preceding pages, there is evidence that the pressure exercised by one twin fœtus upon another or by the parts of a fœtus upon itself may produce teratological results; but it is, at the same time, generally admitted that there is the necessity for the presence of some force which shall press the compressing and compressed parts together, if the theory is to be firmly established on reasonable premises. This naturally leads me to the consideration of the question of the pressure of the umbilical cord and of the amnion.

Funic Pressure.

There are at least two ways in which it may be supposed that the pressure of the umbilical cord may produce teratogenic effects. It may be so disposed around the fœtus as to cause one part of the body to press upon another, or it may itself encircle and constrict one of the parts of the unborn infant. As instances of the former mode of action may be cited G. Barbieri's case (referred to by Taruffi, *Storia della Teratologia*, v. 204, 1889), in which the right hand of the fœtus was kept in apposition to the cheek of the same side by a coil of the cord, with the effect that the ear, the zygoma, and the whole side of the face were deformed; C. M. Daubert's case (*De funiculo umbilicali humano fœtui circumvoluto*, Diss. inaug., Göttingen, 1808), in which the sole of the right foot was brought against the lower jaw by the umbilical cord; and the illustrative examples of L. Heusner (*Arch. f. klin. Chir.*, lix. 206, 1899). It is unnecessary to discuss further this variety of funic pressure, for it is quite conceivable and rational; but the second mode of action of the cord calls for more extended consideration.

May the umbilical cord when coiled round the body or limbs of the embryo or fœtus in utero cause constrictions, arrested developments, and amputations of the parts so encircled by it? This is the question which has for many years called for an answer and led to much discussion and controversy. So great has been the difference of opinion and so large (in consequence) has been the amount of writing upon the subject, that I am compelled to pass over many articles and to collect together the titles of those to which I do refer at the end of this chapter.

The question first arose prominently in connection with the explanation of the curious cases in which a child was born with partial absence of the limbs or with defective development of the fingers and toes. Such cases were well known to writers before the nineteenth century; for Bartholin in 1675, Acoluth in 1740, Maternus de Cilano in 1752, J. U. T. Schaeffer in 1775, Hinze in 1797, and many others put on record instances of different kinds of mutilation of the extremities which had evidently arisen before birth. Maternus de Cilano, to whom I have referred, described an infant born at the seventh month with the right arm defective; he maintained that the case proved that formed parts might be destroyed and absorbed "per energiam autocraticam"; and he ascribed the result to the impression made upon the mother by the sight of a begging soldier without a right arm: the infant lived for eleven weeks, and then gently passed away ("blande expiravit"). The cases reported by Bartholin and Acoluth were also regarded as caused by maternal impressions. Schaeffer's observation was a most interesting one: the infant, a female, born at the seventh month, showed webbing of the fingers of the right hand, and defective formation of those of the left; the right foot had a short hallux, and there was a membranous cord attached to the second toe; the left leg seemed as if it had been amputated below the gastrocnemii, the stump was covered with newly formed cuticle, and from it was suspended by a fibrous cord a small body representing a tiny foot (of the size seen at the third month of intrauterine life) with five toes (Fig. 23). This observation was a most important one, for it answered Haller's objection that a separated hand or foot had never been found in such cases. None of the writers referred to seem to have considered that the pressure of the umbilical cord might have had to do with the congenital mutilations met with. Morgagni, indeed, appears to have regarded funic pressure as capable of fracturing a fœtal limb; but he is silent about its effect in producing antenatal amputations.

Even after the commencement of the nineteenth century, the pathogenesis of congenital defects of the limbs did not include funic pressure as a possibility. F. Chaussier, indeed, found the lower segment of an arm in the fœtal membranes and observed the cicatrised stump, and yet failed to regard the condition as due to amputation, ascribing it to mortification instead. Meckel, however, hinted somewhat vaguely at this possible teratogenic power of the funis umbilicalis in his description of a three months' fœtus, the cord of which had made a groove in the skin over the right scapula, and was twisted round the limbs, which were without fingers and toes. In Jameson's case the death of the fœtus in utero was ascribed to the constriction of the trunk with the umbilical cord; the writer noted the swelling of the upper part of the fœtus and the atrophy of the lower. Watkinson's observation, published in 1825, was in many respects

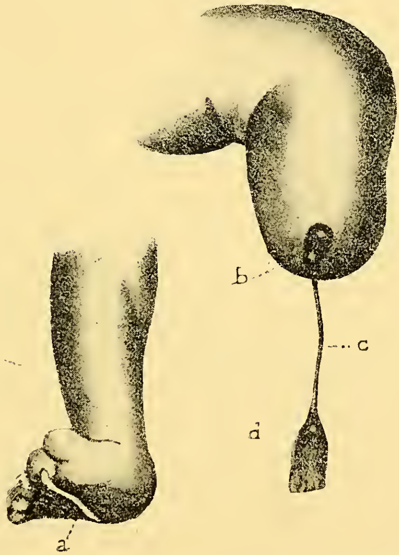

FIG. 23.—Schaeffer's case of Spontaneous Amputation. *a*, membranous cord attached to second toe of right foot; *b*, ends of tibia and fibula of left leg; *c*, membranous cord with *d*, foot suspended by it.

most remarkable. It referred to an infant, born at the seventh month, without a left foot. "I discovered," wrote the author, "that the left foot had been amputated a little above the ankle, and the part nearly, but not quite, healed, in consequence, perhaps, of the bones protruding." He goes on to say: "On examination after the birth, I discovered the foot in the vagina, which I brought away: it also was nearly healed, but here likewise the bones protruded. There did not appear to have been any extravasation of blood from the limb, as far as I was able to judge. This foot (the left) was much smaller than the other, which was rather turned inward; it showed no marks of putrefaction, and, from comparing the two, I am led to suppose that it must have been two months separated from the body." The editors of the Journal in which Watkinson's paper appeared added a rough sketch of the affected parts (Fig. 24). The author gives no explanation of the mode of occurrence of the "amputation" beyond stating that the mother had not been frightened during her pregnancy. It was left for Barzellotti in 1827 to suggest that the umbilical cord, especially if it were unusually long, might become twisted round a limb at an early period in development, might constrict it, cause atrophy of its tissues, and finally cut it through. He was led to this conclusion by the examination of an infant whose limbs consisted of stumps representing about one-third of the humerus or femur; skin of a cicatricial kind covered the ends of the stumps. I have not been able to consult Barzellotti's article in the original,

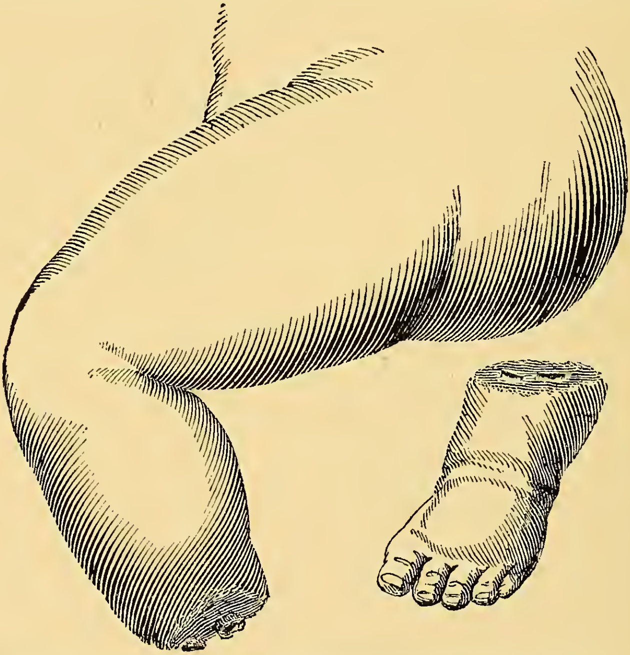

FIG. 24.—Watkinson's case of Spontaneous Amputation of Foot.

but I quote from Taruffi's abstract of it (*Storia della Teratologia*, i. 260, 1881; iv. 89, 1886), from which it appears that Taruffi is justified in claiming for his fellow-countryman the honour of suggesting the teratogenic powers of the funis.

In 1832–33 Montgomery published his short but most valuable papers on spontaneous amputations and circular depressions on the limbs of the fœtus; he, however, ascribed these morbid states to the constricting effects of fine threads or bands of lymph, and not of the umbilical cord. He could hazard no conjecture as to the origin of these threads, but he clearly stated that the circular depressions were intermediate stages which preceded the complete separation of the affected limb. We need not further consider these constricting threads of Montgomery now, for they will be dealt with in the succeeding chapter.

The next incident worthy of note in this relation was the publication, in the United States, of Fitch's case of spontaneous amputation of the right leg; the foot was first expelled, and then two weeks later a fœtus lacking the corresponding foot was born. J. Y. Simpson in 1836 touched upon the action of the umbilical cord in connection with spontaneous amputations; he maintained that it could not produce these effects unless it became fixed in one position round the limbs, but had evidently no difficulty in believing in its constricting power when it was adherent to the underlying parts, and he refers to a case published by Wrisberg in support of this conclusion. In 1837, Montgomery, in his work on *Pregnancy*, returned to the subject of spontaneous amputation in utero, and freely admitted the power of the umbilical cord to produce it; he described two cases, in each of which a three months' fœtus showed indentations in the leg due to the presence of a tight coil of the funis round it. In the succeeding year Schwabe recorded a similar case in Germany; in 1839 Buchanan reported another in America; and Beatty another in Ireland in 1846. Terstesse's observation was not, in all probability, of the nature of a spontaneous amputation.

In 1848 J. Y. Simpson touched upon a very interesting question when he pointed out that there sometimes existed, on the ends of the stumps of these spontaneously amputated limbs, little nodules or projections occasionally bearing nails. He suggested that these indicated an attempt, of a rudimentary kind, to reproduce the amputated extremity, similar to what is seen in many of the lower animals. In 1850 E. A. Martin described a case illustrating Simpson's third possible cause of intrauterine amputation—by fracture: the mother fell from a ladder eight weeks before delivery, and the child was born with the left arm amputated near the shoulder, and the wound still not entirely closed; the separated but nearly full-sized arm was expelled with the placenta.

Thus, by the middle of the nineteenth century, three new theories had come into existence to explain the origin of congenital amputations: by the umbilical cord, by bands of lymph, and by external violence causing fœtal fractures; and the theory with which we are now specially concerned had begun to encounter criticism. As the years went by the criticism was to increase, as we shall see.

The idea that the funis could cut through the tissues of a limb was evidently open to criticism. Martin, as has been stated, doubted its power to act thus unless a fracture of the bone were present; and Gatty pointed out that while the cord might constrict a limb it could not amputate it, because the pressure on the vessels in the cord itself would be so great as to stop the circulation and so kill the fœtus. This objection, however, was somewhat weakened by the publication of J. B. Hillairet's case in which the cord was twisted round the neck of a three months' fœtus; the head was almost amputated, the tissues of the neck being reduced to a pedicle only 1½ mm. in thickness. Weidemann, writing in the same year as Hillairet, apparently did not doubt the power of the cord to cause constrictions, amputations, and death of the fœtus; but Barkow, in 1859, inclined rather to the idea of amputation taking place by means of fœtal gangrene (gangræna fœtalis) comparable to the senile process (gangræna senilis), and Kristeller advanced the idea of an inflammation of the fœtal skin. Chance, also, was a believer in the teratogenic potency of the funis; so was Nebinger; and W. B. Owen related a case in which a fœtus of four months had the legs bound down by the cord in front of the pelvis so closely that they had become embedded in the soft parts of the wall of the abdomen, and one leg was in process of being amputated by the funic pressure.

In 1869, P. Reuss made a valuable contribution to the literature of spontaneous amputations; but, while admitting the teratogenic power of amniotic bands and of pathological processes going on in the skin, he thought that the pressure of the umbilical cord rather tended to cause the death of the fœtus than to produce an amputation. L. Fürst held somewhat similar views; and Barkow, in the same year (1871), examined again, but more in detail, the whole subject of spontaneous amputations, and enumerated four possible causes, namely, external violence, funic pressure, amniotic bands, and fœtal gangrene. Raschkow, in 1872, published a case in which one limb showed the process of amputation going on, the muscles having disappeared and the bone showing atrophy; he endeavoured to meet the objections of Reuss and others by pointing out the rapid growth of the encircled parts (in early fœtal life) and the presence of pulsating vessels in the encircling cord. Gililam's case appeared to demonstrate the deforming power of the cord. Menzel attempted to explain the spontaneous amputation of fingers and toes by a morbid change in the epidermis consisting in a proliferation and downgrowth of the surface epithelium ("epithelial dactylolysis"), a process comparable to that seen in the disease known as ainhum. This view or modifications of it have been advanced by several other writers, including Jeannel (who regarded the amputations as trophic lesions of the nature of scleroderma), Raynaud (ainhum), Longuet (trophic nervous lesion), and Lancereaux (autocopic trophoneurosis). Miram admitted that congenital amputations might be produced in several different ways, but thought that funic pressure was seldom the active factor.

Within recent years the theory of the deforming effects of convolutions of the umbilical cord cannot be said to have gained strength, although J. Cleland, E. Viehöfer, E. Pestalozza, F. Merkel, R. Lhomme, Turgard, C. Tournier, M. Duval, J. Roubinovitch, and many others admit its possibility, and would give it a place in the pathogenesis of deformities of the limbs if not of actual amputations. On the other hand, B. Thompson Lowne, C. Dareste, and the supporters of the theories of nerve influence, etc., are sceptical. It must be confessed that there are obvious difficulties in the way, which make it difficult to understand how a structure like the umbilical cord can cut through a part of the body like an arm or a leg; at the same time it must be borne in mind that the possibilities of pathological activity and of physiological repair in the early periods of antenatal life are not fully known to us and may be much greater than is commonly supposed. Again, if we admit the power of bands or threads of amniotic tissue to perform amputations in utero (as most teratologists do), it is only a step further to ascribe a similar potentiality to the umbilical cord. Possibly it may be necessary, for the full exercise of this morbid action of the cord, that the underlying skin develop pathological changes; but this only diminishes the amount of responsibility, so to say, that the cord has in the results produced, and does not entirely free it from participation. Finally, it may be said that the power of funic pressure to produce grooves and scars on the limbs and body of the fœtus and to interfere with the nutrition of distally situated parts can hardly be doubted, and that, in the absence of exact knowledge regarding the possibilities of pathological processes in embryonic life, it cannot be definitely stated that the cord is incapable of actually producing the amputation of a part.

I have, in this chapter, given a sketch of the pressure-theories of teratogenesis, and have shown how there has been a progressive tendency to minimise the causal factor involved, as more and more light has been thrown upon antenatal problems. I have not, it is true, yet considered the theory of amniotic pressure in teratogenesis, for that is more conveniently and correctly discussed with the theories of *disease* as a cause of monstrosity and malformation, but it also has of late years been thrown somewhat into the shade by the inquiry into the causes which produce the amniotic tightness and the amniotic bands. This will become evident to the reader after he has perused the following chapter. For all these reasons I have placed the theory of traumatism and pressure first among the teratogenic theories of the present; to my mind it comes nearest to the views of the past and is furthest removed from the most advanced conceptions of the day. This does not by any means imply that it contains no truth, neither does it exclude it as a probable explanation of some at least of the monstrosities which are met with.

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CHAPTER XI

The Nosological Theory in Teratogenesis: Fœtal Diseases as Causes of Monstrosities, the Theory and its Critics; Disease of the Fœtal Annexa as a Cause of Monstrosities; Amniotic Disease in Teratogenesis; the Amniotic Theory and its Developments; the Facts and the "Fancies," the Adherents and the Critics of the Theory; Congenital Amputations and Fœtal Skin Diseases; Regeneration of lost Parts; Conclusions; Literature.

The idea that the diseases of the fœtus or of its investing membranes may be the cause of monstrosities is not to be reckoned among the theories of the past; it is indeed a theory of comparatively modern times without even roots in the past; it may in some respects be called the teratogenic theory of the nineteenth century. It is not, however, on that account an accredited view at the present time, and several teratologists, including Taruffi and M. Duval, have declared against it. In this respect the older authors and the most modern are in accord; but it does not on that account follow that the former reached their conclusion by the same process of reasoning as the latter. Probably the older writers on monstrosities were so impressed with the altogether special and peculiar features of teratological phenomena that it never entered their mind that they could possibly be due to diseases, and so they kept silence on that point.

The idea that diseases are the causes of deformities may be called the *nosological* or *pathological* theory of teratogenesis; the former name more correctly expresses what is meant, although the latter has a less unfamiliar appearance. There are two views contained within this one theory: according to the first, the fœtus itself is the subject of diseases which produce the malformations; according to the second, it is through disease of the fœtal membranes and more particularly of the amnion that anomalous conditions are set up in the fœtus or embryo. It will be convenient to consider these two aspects of the nosological theory separately; since the notion that regards fœtal maladies as the causes of monstrosities is older than that which ascribes teratogenic powers to the diseased amnion, it will be dealt with first.

Fœtal Disease in Teratogenesis.

Very little is heard of the nosological theory in teratogenesis before the middle of the eighteenth century. Licetus, however, who wrote in 1616 (*De Monstris*, lib. ii. cap. viii.), had a short chapter on the subject. In it he pointed out how in adults certain diseases such as syphilis might have deforming effects due to destruction of tissues (*e.g.* in the case of the nose and penis); and he suggested that, in the more tender fœtus, inflammations and corroding humours might lead to the consumption of a hand or a foot. If the vis medicatrix naturæ were effective, the mutilated part would cicatrise and so a monster would be produced. "Sic igitur ex vi morbi oriuntur pleraque monstra mutila," he said in conclusion.

In 1741 J. B. Bianchi published a noteworthy work (*De Naturali in Humano Corpore, Vitiosa Morbosaque Generatione Historia*, Augustæ Taurinorum, 1741); in it he discussed the possible causes of monstrosities ("causæ autem," he wrote, "eheu nimiæ!" recognising that perplexing plurality of etiological factors which my readers already know so well), and referred specially (on p. 242) to diseases of the fœtus and their deforming effects, such as the production of infants with tails, beaks, and claws, or covered with hair. Bianchi's conception of how these deformities arose was not, however, very clear, and it was reserved for Morgagni to frame a rational and scientific explanation of the possible *modus operandi* of diseases as causes of deformities. In his great work, *De sedibus et causis morborum*, published in 1761, Morgagni dealt with many matters in an epoch-making manner, and among these was the theme of monstrosities. "What I shall say here," he wrote (I quote from B. Alexander's translation of 1769, vol. ii. p. 751), "will be rather what relates to the observations themselves than to the controversy which is agitated in this age" (he refers to the Parisian discussion, *vide* p. 133), "among very learned men, in regard to the origin of these monsters"; nevertheless he treated of their origin also and in more luminous fashion than the "very learned men." Here is his account of the manner in which he believed that anencephaly was produced from hydrocephalus (vol. i. p. 251): "Doubtless the force of the water, gradually collected in a hydrocephalus, especially if the fœtus be tender, is very urgent and manifest, and the more so in proportion as it begins the sooner to act on the less resisting parts of the cranium. And hence the approach of the bones to each other is not only impeded, but also the very growth of them, sometimes in a few, and sometimes in the greatest parts; so that they seem to be entirely wanting." In another passage, Morgagni, in writing of an anencephalic fœtus, further defined his theory: "Here then you have a description of no common monster; but of a hydrocephalous monster: so that after you have set down as many things as you please, to the account of the monstrous condition; yet still more circumstances will remain, that you must attribute to the impelling force of the water, such as the obstructed growth of some of the bones of the cranium, the depression of some, the impelling of some to one side, and the drawing asunder of others."

Dareste (*Production artificielle des Monstruosités*, p. 17, 1891) claims for Marcot of Montpellier the honour of having been the first to suggest this theory of causation of anencephaly, and quotes his article published in 1716 ("Mémoire sur un enfant monstrueux," *Mém. de l'Acad. roy. des sc. de l'année* MDCCXVI., p. 329, Paris, 1741). On referring to Marcot's article, I find that he does indeed very clearly state that he regarded the disappearance of the parts of the brain in anencephaly as due to hydrocephalus; he thought that the pressure of the serous fluid upon the blood vessels going to the brain hindered the nourishment of that organ, and so led to its diminution. The pressure acted most upon the internal carotid arteries, and so an excess of blood found its way into the external carotids and led to the lividity of the neck and face and to the swelling of the eyelids. What really puzzled Marcot was how the fœtus could have lived in utero without the brain which furnished the animal spirits—"c'est ici veritablement où se trouve le noeud de la difficulté"; he was forced to leave this difficulty unanswered. It would seem at first sight as if Dareste were right in giving Marcot the honour of first proposing this theory of the origin of anencephaly, inasmuch as the year 1716 certainly preceded 1761; but the question of precedence is not thus easily settled, for I find that Taruffi (*Storia della Teratologia*, vi. 150, 1891) cites a much earlier work of Morgagni (*Adversaria Anatomica*, Bononiæ, 1706) as that which contained the first statement of his views on the causation of anencephaly. So the honour returns to Morgagni after all.

The idea of *diseases* as the causes of monstrosities, once enunciated, rapidly gained supporters. Before referring to other kinds of disease which have been believed to be teratogenic, I may rapidly sketch the history of the theory that hydrocephalus produces anencephaly, for it was, as I have shown, that with which Morgagni's name was specially associated. In the early part of the nineteenth century, C. W. Schlegel and K. A. Rudolphi (cited by Ahlfeld, *Die Missbildungen des Menschen*, p. 284, 1882) reported instances in human embryos (about six weeks old) in which a dropsical vesicle was found in place of a brain; these were regarded as representing the stage of development of anencephaly prior to the rupture of the hydrocephalic sac. Tiedemann (*Ztschr. f. Physiol.*, iii. 36, 1829), also cited by Ahlfeld, described the case of a fœtus with a dropsical brain covered only by a membranous sac; this observation might perhaps be adduced in support of Morgagni's view. Ryan (*Lond. Med. and Surg. Journ.*, vii. 77, 1835) wrote as follows: "It is easy to understand that the serosity or water, as it is improperly called, may distend the brain, rupture its membranes, separate the bones of the cranium, burst the scalp, and finally escape into the amniotic fluid. The whole brain, membranes, bones, and scalp are destroyed by absorption, and the base of the skull alone remains, forming the acephaly." In another place (p. 175) he stated that "hydrocephalus may advance rapidly, burst the cranium, and produce anencephaly or microcephaly." Ryan's views on this subject are, therefore, quite clear. V. Portal's record of a twin labour in which one fœtus was hydrocephalic and the other anencephalic (as cited by Taruffi, *Storia della Teratologia*, vi. 151, 1891) forms an interesting although indirect piece of evidence in favour of Morgagni's opinions. Otto (*Monstrorum Sexcentorum Descriptio*, Introduct. pp. xv–xviii, Vratislaviæ, 1841) discussed the effects of various degrees of distension of the cerebral ventricles, and pointed out that the nervous system was not only very fragile but was also the first part to appear in the embryo; it was therefore very apt to be injuriously acted upon and to have its evolution retarded or misdirected; most monstrosities except those characterised by excess of parts were due to diseases. Förster (*Die Missbildungen des Menschen*, 2 edit., p. 77, 1865) arranged the results of the accumulation of fluid in the cerebro-spinal canal into three groups (1, hydrocephalus and hydrorrhachis; 2, hydrencephalocele and hydromyelocele; 3, cranioschisis and rhachischisis), according to the degree of distension and destruction of parts.

At a meeting of the Edinburgh Obstetrical Society in 1847 (*Month. J. Med. Sc.*, n.s., ii. 215, 1847[1]) J. Y. Simpson stated that, in his opinion, the malformation in anencephalous monsters arises from intrauterine disease, namely, from the bursting of the head when hydrocephalic. In another place (*Obstetric Memoirs and Contributions*, ii. 199, 1856) he wrote: "Though assuredly this doctrine has been carried far beyond its just limits by some of the authors here alluded to (Morgagni, Penada, Tiedemann, Béclard, Dugès), there is still, however, as we believe, much reason to suppose that one or two varieties of anencephalous malformations are truly referable to the purely physical effects of hydrocephalic inflammation and effusion." But to Simpson's contributions to the nosological theory of teratogenesis I shall refer again immediately.

F. Ahlfeld (*Die Missbildungen des Menschen*, pp. 284–290, 1882) thought that while some few cases of anencephaly might be due to amniotic adhesions, most were caused by hydrocephalus, and he added that the bursting of the hydrocephalic sac could not occur before the fourth week of embryonic life; the probable reason for this reservation is (as Taruffi points out, *op. cit.*, vi. 151, 1891) that before the fourth week the eyes, which are often well formed in anencephaly, are not independent of the part of the brain which is destroyed. Alfred W. Hughes, in an article on the central nervous system and axial skeleton in anencephalous monsters (*Lancet*, ii. for 1887, p. 1212), was struck with this difficulty, for he found well-developed eyes with optic nerves, although only the parts originating in the posterior cerebral vesicle seemed to be represented; he thought, therefore, that all the vesicles at one time underwent a certain degree of development which afterwards became aborted, and gave place to retrogressive changes. Cleland (*Journ. of Anat. and Physiol.*, xvii. 257, 1883), in a well-considered contribution to the study of spina bifida, encephalocele, and anencephalus, came to the conclusion that while the open condition of the cerebro-spinal canal might be due to non-closure of its walls, it was probable that anencephalus was due to rupture after the primary optic vesicles were cut off from the cerebral vesicles. Many other writers (*e.g.*, Doran, *Trans. Obst. Soc. Lond.*, xxxi. 52, 1890) have supported Morgagni's views of the origin of anencephaly and allied states; and I myself, in referring some years ago to a case in which a man begat a hydrocephalic child by his first wife and two anencephalic fœtuses by his second, stated that I thought the occurrence might have some bearing upon the theory that anencephaly is due to early hydrocephalus (*Trans. Edinb. Obst. Soc.*, xvii. 228, 1892). It must, however, be admitted that there are many difficulties in the way of the full acceptance of the theory, and to these the attention of the reader is now turned. It may at the same time be noted that H. Ribbert's observation of two cases of rupture of the cranium in embryos of the goat and cow is evidence in support of Morgagni's contention (*Arch. f. path. Anat.*, xciii. 396, 1883).

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[1] This reference is erroneously stated in Simpson's *Obstetric Memoirs*, both the name of the journal and the number of the page being wrong; defective references are as "pin-pricks" to the earnest student, and he is often thus maltreated.

The criticism to which Morgagni's theory of the causation of anencephaly was subjected was no doubt in large measure due to the unjustifiable extension of the view to the explanation of many other, in fact of most other, monstrosities and malformations, with the exception of those in which there was excessive development. It was the expansion of the theory that suggested its defects and excited criticism, not without cause, as every one must admit. Let us consider some aspects of this expansion.

Béclard (*Bull. Fac. de méd. de Par.*, v. 488, 1816–17) insisted that dropsy was one of the most frequent diseases of the fœtus, being produced by twisting of the cord, obliteration of one of the umbilical arteries, etc.; it most commonly affected the head and brain, and might then give rise to a hydrencephalic hernia, to spina bifida, or to anencephaly, according as it occurred late or early in intrauterine life. Thus far Béclard simply repeated the views of others, but he carried his opinions much further: he thought that destruction of the olfactory nerve would cause the atrophy of the ethmoid bone and the union of the two eyes, that destruction of the medulla oblongata and its nerves would lead to loss of the face, that the diaphragm would be wanting if its nerve were involved in the common destruction, and that in like manner the arms, the thorax, the abdominal walls, and even parts of the feet would disappear as the dropsical ruin of the nervous system extended downwards. In this way Béclard explained the origin of cyclopia, of otocephaly, of paracephaly, and even of acephaly; and in this view he was fully supported by A. Dugès (*Ephém. méd. de Montpel.*, ii. 132, 275, 1826; *Rev. méd. franç. et étrang.*, iv. 407, 1827). Another development of the nosological theory was seen when A. Velpeau (*Mém. Acad. roy. de méd., Par.*, iii. 90, 1833) attempted to explain exstrophy of the bladder and its associated malformations by the occurrence of a slight erosion of the anterior abdominal walls in the hypogastric region which gradually deepened and finally involved the bladder. B. Phillips (*Cyclopædia of Anatomy and Physiology*, i. 392, 1835–36) defined the process and its steps more particularly when he stated that the disease began as an ulceration or perforation of the penis or of the hypogastrium, and that the bladder was secondarily involved. The same sort of explanation was given for the so-called spontaneous amputations of limbs by Chaussier (*Discours prononcé en 1812 à la distribution des prix de la maternité*) and others.

Yet another development of the theory that fœtal diseases are the causes of monstrosities took place in connection with fœtal peritonitis. J. Y. Simpson, in an article on peritonitis in the fœtus, published in 1838 (*Edinb. Med. and Surg. Journ.*, vol. l. p. 390, 1838), hinted that "to these fœtal diseases, and more particularly to certain degrees of inflammation, might yet be traced the origin of various morbid states, the true nature of which is at present little suspected." In the following year he returned to the subject, and brought forward evidence to prove that various congenital herniæ (umbilical, diaphragmatic, and inguinal) are due to fœtal peritonitis; that various malformations, both in the way of displacement and of arrested development, in the digestive, urinary, and genital organs, are indirectly caused by the same malady; and that inflammatory action in the other serous cavities (pericarditis and pleuritis) may lead in the same manner to malformations among their visceral contents (*Edinb. Med. and Surg. Journ.*, vol. lii. p. 17, 1839). The word "indirectly" in the above paragraph must be specially noted, for Simpson was too perspicacious and keen-sighted not to realise that the nosological theory was insufficient in itself to explain several of the malformations with which he was dealing. He referred to the "happy idea that was first suggested by the master mind of Harvey, relative to certain malformations consisting, *not* in the *substitution* of an entirely new and anomalous type of structure in the malformed part, but only in the simple *permanence* of some of its fœtal types," and then proceeded to work into Harvey's "happy idea" his own no less happy idea that "the state itself of impeded development might be traced to the anterior influence of different inflammatory and other casual pathological conditions of the early embryo." It seemed probable to him also that "a limited series of those malformations that are now looked upon as the decided results of arrested development may come again to be regarded, as they were formerly, not as instances of absolute want of development of the defective part, but as cases in which this part had been, in the first instance, more or less fully evolved, and then subsequently destroyed by morbid action." It will be seen, therefore, that Simpson greatly strengthened the nosological theory of teratogenesis by including in it that of arrested development; in this way he gave to it a more scientific aspect, and answered several of the objections which had been brought forward against it. It does not, however, appear to have entered into his mind that the arrestments could have arisen otherwise than through preceding diseases either of the fœtus or of its membranes. In this respect only did he fall short of holding the most advanced views on teratogenesis which prevail at the present day.

Before I pass to the consideration of the criticisms which have been advanced against the nosological theory, I must devote a paragraph to a notice of the opinions of Jules Guérin; these were stated on various occasions between the years 1838 and 1880, and summarised in his large work (*Recherches sur les difformités congénitales chez les monstres, le fœtus, et l'enfant*) in 1880. He brought together a great mass of facts from various sources along with not a few personal observations; and he argued from these, not without the suspicion of special pleading, that the disease of the fœtus which is the cause both of monstrosities and of the minor malformations which accompany them is a general or local affection of the nervous system. He also laid great stress upon the occurrence of convulsive muscular retraction or contracture as one of the steps in the process which ended in the production of teratological phenomena, major and minor. According to his theory, a large number of monstrosities and malformations, including suppressions, arrestments, and perversions of development, were due to one great cause, an affection of the cerebro-spinal system. He certainly lost no opportunity during a long series of years of bringing his opinions prominently forward, and he claimed that he had converted that famous teratologist, Geoffroy Saint-Hilaire, to his way of thinking. This conversion took place, as Guérin tells us, at the meeting of the Parisian Academy of Sciences in 1840, on the occasion of his reading there his contribution entitled "Essai d'une théorie générale des difformités articulaires chez les monstres, le fœtus, et l'enfant." The incident I give in Guérin's own words: "Aussitôt ma lecture terminée, il vint me trouver à mon banc et me dit à haute voix: J'avais tort et vous avez raison" (*op. cit.*, p. 174). All this and much more in the way of the application and extension of the doctrine referred to will be found in Guérin's large book already named. It may be added that P. E. F. Delplanque, in his *Études Teratologiques* (Lille, 1885), looked to an intrauterine disease of the fœtal nervous system (of the nature of tetanus) as the cause of the curious bovine malformation known as the calf with a dog's head.

It is now time to consider some of the criticisms which were provoked by the nosological theory in teratogenesis and its expansions, ramifications, and ultimate developments. P. Vannoni (*Gaz. med. ital. feder. tosc.*, 2 s., i. 218, 1850), for instance, pointed out that changes in the cerebro-spinal system failed to account for the variety of forms of monstrosity, and that many of the alleged causal agents were obviously incapable of producing any kind of monstrosity at all. He did not, however, deny that the morbid state and its results might suspend, alter, or divert the organic processes so as to lead to fissions, to asymmetry, and to other deformities. Vannoni, therefore, did not criticise so much the theory that hydrocephalic distension of the cerebro-spinal canal produced rupture and resulting anencephaly and spina bifida, etc., as its wide and somewhat rash enlargements and amplifications. Perls, however, did not hesitate to animadvert upon the theory as it dealt with anencephaly itself, and thus to attack the view in what had been considered its strongest position. He pointed out (*Lehrbuch der allgemeinen Ætiologie und der Missbildungen*, 282, 1879), from the examination of twenty-seven specimens, that the basis cranii in anencephaly shows a convexity and not a concavity, or at least a flattening such as is found in hydrocephalus. If hydrocephalus is the cause of anencephaly we should expect to find not a convexity but a concavity of the cranial base; but, as a matter of fact, we discover, according to Perls, signs not of an internal expanding force but of a pressure acting from without inwards. A much older criticism than that of Perls was brought forward by Gall and Spurzheim, and repeated by Etienne Geoffroy Saint-Hilaire (*Philosophie anatomique des monstruosités humaines*, p. 152, Paris, 1822), who pointed out that the perfect state in which one often found the delicate structures lying on the base of the skull in anencephaly (*e.g.*, the auditory, olfactory, and optic nerves) was an argument against the production of that monstrous condition by internal pressure. "Comment eussent-ils pu résister à l'action d'un fluide qui aurait dissous des os si durs, des membranes si tenaces?" Another argument was found in the well-nourished state of anencephalic fœtuses at the time of birth—surely if in the early weeks of intrauterine life the fœtus were the subject of such a serious disease as hydrocephalus it should be born weak and puny! The younger Geoffroy Saint-Hilaire (Isidore) in his *Histoire des Anomalies* (vol. iii. p. 518, 1836) gave other reasons which led him to reject the theory of hydrocephalus as the cause of anencephaly, among which were the facts that the bones of the cranial vault were equally reduced in all their dimensions and not truncated and incomplete, that the bones of the basis cranii were complete but badly formed, and that the vertebral laminæ were not simply partly destroyed but were also displaced laterally and spread out: these characters, he thought, pointed to an arrest of development and not to the destructive action of hydrocephalic fluid within the cranium. We have it, however, on the authority of Guérin (*vide supra*) that Saint-Hilaire resiled from this position in after years. At the same time it must be admitted that the arguments against the hydrocephalic theory of origin of anencephaly possess considerable weight, and that the weight is not greatly lessened by supposing that the rupture of the cranium would so relieve the pressure upon the cranial base as to cause a convexity to take the place of a concavity (Virchow, *Untersuchungen über die Entwickelung des Schädelgrundes*, p. 102, 1857; Ahlfeld, *Die Missbildungen des Menschen*, p. 291, 1882). Among recent writers who have opposed the nosological theory of teratogenesis, both in its wide application and its special relation to anencephaly and spina bifida, are Dareste and Duval. The former (*Production artificielle des monstruosités*, p. 54, 1891) insists that both the pressure-theory as commonly held and the theory of diseases as the causes of monstrosities are founded upon erroneous conceptions of embryogenesis; those who have held these views have sought for the explanation of teratological occurrences in the embryo without knowing how the embryo itself is formed. In regard to the special and so oft-quoted case, anencephaly, Dareste (*op. cit.*, p. 385) ascribes its development to an arrest in ontogenesis; the medullary groove either does not close at all or does so too late, with the result that the upper wall of the cerebro-spinal canal is composed of an ectoderm which does not give origin to nervous tissues; serum continues to accumulate in the tube, and so a state of dropsical distension in the embryological but not in the pathological sense of the word is produced. Duval (Bouchard's *Traité de pathologie générale*, i. 181, 1895) holds similar views; he admits that in exencephaly and pseudencephaly there is an accumulation of fluid in the cerebral ventricles, but asks pointedly whether this circumstance is to be regarded as a cause or a consequence of the arrest of development of the walls of the cerebral vesicles; he himself has evidently no doubt that it is a consequence, and not a cause. Vaschide and Vurpas (*Nouv. iconogr. de la Salpêtrière*, xiv. 388, 1901), in their admirable article on the histology of the nervous system of an anencephalic fœtus, indicate their belief that there had been cerebral hemispheres in this case at an early period of embryonic life, and that these had disappeared, being converted into the vascular new formation found on the basis cranii; there were signs of a very active and intense inflammation affecting the nerve tissues, the meninges, and the vessels. These authors are evidently impressed by their discoveries, but they do not comment upon them, promising to return to the subject of their bearing upon teratogenesis in another article.

My views on this subject of the relation of diseases to monstrosities I have already indicated in Chapter VII.; but I shall return to the matter more in detail after I have sketched the second aspect of the nosological theory, that which looks to diseases not of the fœtus itself but of its membranes for the causal factors in teratogenesis.

Disease of the Fœtal Annexa in Teratogenesis.

There is no very clearly marked line dividing the one aspect of the nosological theory in teratogenesis from the other; the transition from the idea of fœtal diseases as causes of monstrosity to that of diseases of the fœtal annexa in the same relation is an easy one. Authors are not always careful to separate the two notions, and so they are sometimes found side by side in the explanation of the origin of a malformation or monstrosity. The annexa of the embryo and fœtus are the amnion and chorion, the umbilical vesicle, and (perhaps) the allantois. Doubtless, diseases of any of these structures may exist, but in relation to teratogenesis little has been advanced regarding any of them save the amnion. It is true that J. Y. Simpson, in 1836, wrote of the malforming effects of placental inflammation (placentitis) upon the fœtus; but he referred not so much to disease of the chorionic villi and decidua serotina, which go to form the placenta, as to inflammation of the amnion covering its fœtal aspect; it was really amniotitis, and not placentitis, that Simpson described and meant. There is no need, therefore, for us to delay our consideration of the theory of disease of the amnion as the cause of monstrosities. It is practically the only theory that we require to deal with.

Amniotic Disease in Teratogenesis.

In the pathology of the embryo, the amnion is believed to occupy the same dominant position that the placenta does in connection with the pathology of the fœtus. It is, or rather it is held to be, the chief cause, direct or indirect, of all those malformations or monstrosities that are characterised by defective development. At the same time, all teratologists do not by any means view its mode of action in the same way; as a matter of fact, they look at it in a number of very different ways. The idea of disease of the amnion as the cause of teratological results is not the only amniotic theory of teratogenesis; there is the idea of pressure of the amnion as the cause of malformations; there is also the notion of arrested development of the amnion as the chief factor in teratogenesis. There are, then, three amniotic theories, and not one. Further, these three views of disease, pressure, and arrested development of the amnion have become so combined, coupled, connected, and as it were confederated together, that their disentanglement has come to be an almost impossible process. In the description which follows I shall not indeed try rigidly to dissociate them from one another, for to do so would lead to unnecessary repetition, and would not tend to make a complicated subject any less complicated. At the same time I shall endeavour to keep the notion of amniotic disease rather than that of pressure or of arrested development prominently before the reader.

There are two parts of this theory, as of all theories, namely, the records of the cases which have been observed and the reflections that the observers have made upon them; the facts and, one had almost said, the fancies. About the former there can be no reasonable doubt, always granting the knowledge and good faith of the fact-recorder; with regard to the latter there may be the most varied opinions and estimates according to the acumen and discriminative penetration of the critic. Theories, also, which seemed at one time to fit the facts may, with the discovery of fresh facts and with advances in the method of regarding them, cease in any degree to explain them satisfactorily. This has happened not once but several times with the amniotic theory in teratogenesis, progress in the allied subjects of Embryology, Biology, and Pathology having called for a revision of current views. Let us, in the first place, consider the facts, and thereafter deal with the theories.

The facts are of different kinds, and to be intelligible they must be stated with some degree of fulness. The reader must not be impatient of details at this stage in his study of Antenatal Pathology, for he is now approaching some of its deepest problems and most hidden mysteries; he is entering into the penetralia or inmost recesses of teratogenesis. Let him be resigned while the facts are being marshalled.

The *first* detachment of facts contains the observations that have been made upon adhesions between the cranium or face of the fœtus and the amnion. Since in many of these cases the adherent part of the amnion has been that covering the fœtal surface of the placenta, the observers have described them as instances of adhesion of the head to the placenta; no objection need be taken to the nomenclature so long as it is borne in mind what the actual facts are. More than fifty cases of this kind have been collected together by Taruffi (*Storia della teratologia*, i. 270, 1881; v. 298, 1889; viii. 59, 1894), and I have found some additional records. Further, I have been able to examine two fœtuses showing various malformations

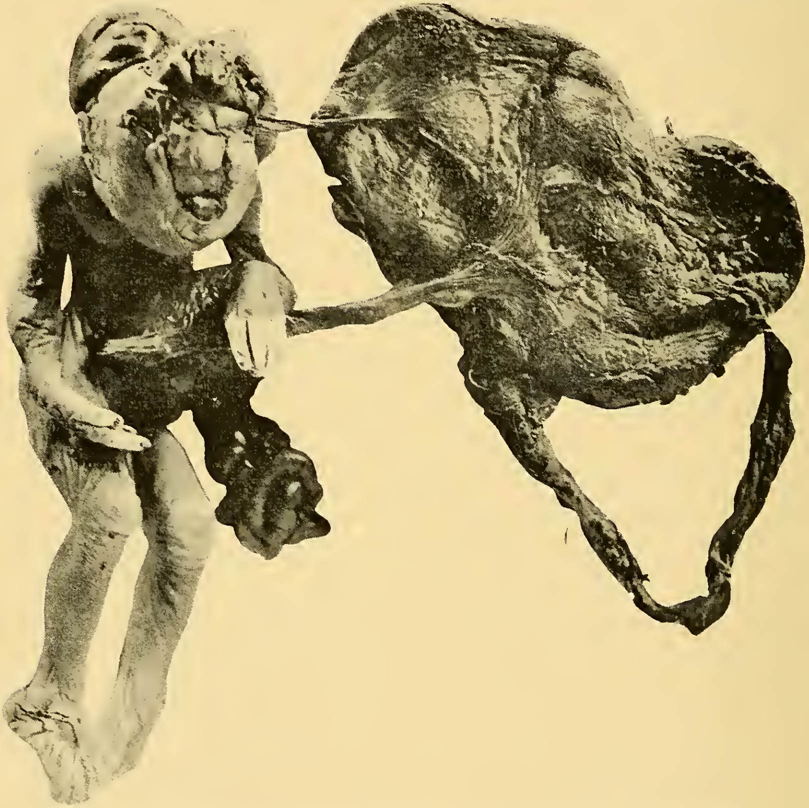

Fig. 25.—Fœtus showing amniotic adhesion to forehead, double facial fissure, and exomphalos. Specimen No. 300.

associated with adhesion of the head to the amnion covering the placenta; in one of these instances the specimen came into my possession with the afterbirth still attached to the fœtus, leaving therefore no room for doubt as to the exact nature of the case. For this interesting monstrosity (Fig. 25) I am indebted to Dr. S. H. Richards, of North Ormesby, Middlesbrough, from whom I received it in March 1903. It was the product of a five months' pregnancy; the mother, a II-para whose first pregnancy ended in the birth of a normal infant fell off a table and badly bruised her side when two months advanced in gestation; there was at the labour a large amount of liquor amnii, and it was stated that before the quickening the abdomen had been larger than usual and had thereafter diminished; the shoulder of the fœtus and the placenta presented together, and the latter and the whole fœtus (a female) came away at the same time. There was no osseous cranial vault, and the brain projected as a bilobed mass covered only by the membranes; there was a double facial fissure, and the eyes were malformed; most of the abdominal contents were outside the abdominal cavity (exomphalos); the umbilical cord, five inches in length, was inserted as usual into the fœtal aspect of the placenta; the fœtal membranes were somewhat torn and disarranged; and from the amnion over the placenta a distinct band, showing some twisting, passed to the cerebral membranes above the left eye. There was a circular groove round the right upper arm, and both feet were clubbed. By a curious coincidence I had received from Dr. T. J. Thomson, of Edinburgh, an almost exactly similar monstrosity not many days before Dr. Richard's specimen arrived; this (Fig. 26) was an eight months' fœtus with exomphalos, a single facial fissure (right side), absence of the cranial vault, and malformation of the right hand; unfortunately the placenta was not available for examination, but the head and upper part of the fœtus were surrounded by strands of membrane continuous with the cerebral membranes and peritoneum, and it is probable, therefore, that in this case also there had been extensive amniotic adhesions.

Cases resembling the two above described have been reported, as has been said, in considerable numbers. One of the oldest observations was that made by Paul Portal[1] in 1671 and published in 1685. He was called to a labour case, and found the infant presenting by the back of the neck; he turned and delivered, and discovered that the fœtus was monstrous. It was a female, and had attached to the head a large sac from which a band of membrane passed to the fœtal surface of the placenta; there was a hare-lip (median in position according to the illustration); the right hand lacked the ring finger and the left arm was shortened; the feet were clubbed. The umbilicus, however, was normally closed. To his record the author adds the reflection that one often sees strange things at confinements, and "on peut dire que la Nature se joue dans la generation." Another early observation was that of Adam von Lebenwaldt, published in 1690. His record was entitled "Singularis Amnii cum fœtu cohæsio"; it was so brief that I may give it here verbatim: "Scriptum mihi est a Viro fide digno in Diœcesi Salisburgensi natum fuisse infantem, cui membrana amnios per totum caput, faciem usq; ad pectus arcte conjuncta fuit; dum circa os et labia secaretur, infans linguam exporrexit et per unum diem vixit." Von Lebenwaldt is truly so laconic that he leaves us in doubt as to the state of the fœtus, although he finds room to tell us that it put out its tongue! Possibly the "man worthy of trust" who saw the case did not know the details.

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[1] *Vide* bibliographical list at the end of this chapter for this and other references.

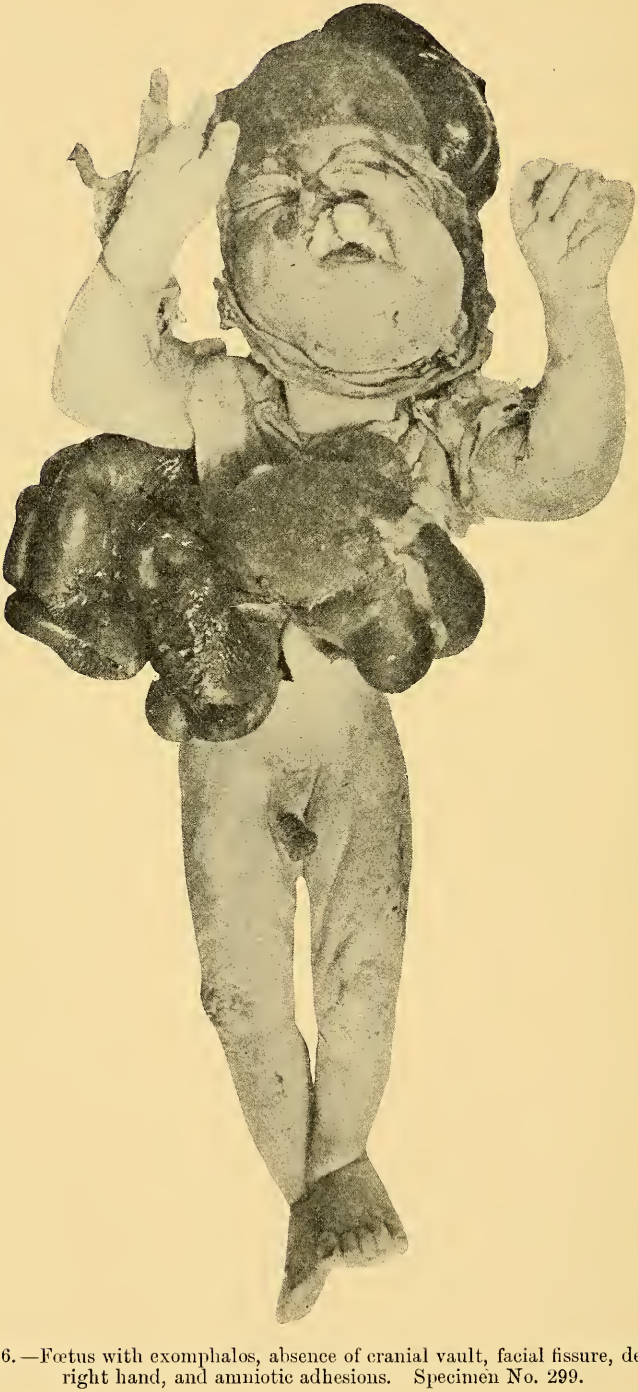

FIG. 26.—Fœtus with exomphalos, absence of cranial vault, facial fissure, deformed right hand, and amniotic adhesions. Specimen No. 299.

A few cases were reported in the eighteenth century, and in 1800, T. Pole, Surgeon and Lecturer upon Midwifery, London, described a typical instance. The infant had been born as a footling, and had lived for thirty-six hours. The bones of the cranial vault were absent, a large sac (cerebral hernia) occupying the summit of the head; there was a facial fissure and a split nose; and the middle finger of the right hand was defective. The placenta was attached to the upper part of the child's head, the largest portion lying over the occiput and scapulæ. Pole had not before seen a case of placental adhesion to the head, but he reflected that "Nature is, however, so frequently regardless of her common laws, as to deviate in such an endless variety, that the best informed man can have no adequate idea of the diversity of her productions." He seems to have ascribed the condition of the cranium and placenta to inflammation of two surfaces in contact with each other, followed by adhesions.

It is unnecessary to describe in detail any further cases, for they all have a certain family resemblance. Among the more noteworthy of them may be named those reported by T. C. Cam, E. Geoffroy Saint-Hilaire, J. F. Meckel, Cerutti, Rudolphi, J. Y. Simpson, Robert Lee, A. G. Otto, Pies, Rayer, Houel, Heyfelder, Barkow, Förster, Virchow, Jensen, Charvet, Walker, Hager, C. E. Stein, Hein, Bassett, Bogatsch, Fromm, Baacke, Broca, Guéniot, Jester, Krumrey, Debierre and Lambert, Fronhöfer, H. N. Robertson, Fleischer, Jacobs, and Veith. From these cases we may draw certain general conclusions regarding cephalic adhesion of the amnion. The bones of the cranial vault are usually absent, and most commonly there is no proper scalp, the brain being covered only by its membranes; in many instances there is also encephalocele or hydrencephalocele as well; in a few cases there is absence of the brain (anencephaly). The amnion on the placenta or bands proceeding from it are usually attached to the membranes covering the more or less altered brain; but sometimes the amniotic connection is formed with the face, which then shows malformations. The facial deformity generally takes the form of hare-lip or facial fissures; in the latter case the fissure, which may be unilateral or bilateral, passes from the mouth to the orbit, and sometimes has the amnion attached to its margins. The nose and eyes may also exhibit various deformities. The malformations are not necessarily limited to the region of the head, for the anterior abdominal and thoracic walls may be defective and allow the protrusion of several of the viscera; further, the extremities not unfrequently show such anomalies as absence of digits or parts of digits, so-called congenital amputations, club-feet, and circular or oblique grooves. A limb may also be fixed to some part of the body, even to the head, by a band. The umbilical cord is usually shorter than normal.

A *second* detachment of the facts regarding the amniotic factor, which I am now marshalling, contains the cases in which the abdomen of the fœtus is the part most obviously affected. In these cases the amnion is generally attached to the margins of a more or less large opening or defect in the anterior or lateral abdominal wall.

I have been able to examine several specimens of this type of monstrosity. One of the most typical of them (Fig. 27) was the six months' female fœtus given to me for examination by Dr. Ballantyne, of Dalkeith, and briefly described by me in the *Transactions of the Edinburgh Obstetrical Society* (vol. xvii. p. 241, 1892). The case was a footling, and, as there was some hæmorrhage going on, the labour was quickly terminated by traction on the feet; during the extraction of the fœtus a sac was ruptured, and this sac, which had been taken for the bag of membranes of a second child, was found to be made up of amnion adherent to an opening in the anterior abdominal wall and continuous with the peritoneum. The sac contained several of the abdominal viscera (liver, spleen, stomach, large and small intestine) as well as the heart, for the diaphragm was defective; there was no separate umbilical cord, for the vessels ran in the wall of the sac directly to the membranes to be inserted near the centre of the placenta, and had a length of not more than twelve centimetres. In addition to the exomphalos thus produced, the fœtus showed anencephaly, spina bifida affecting the whole spine, and marked

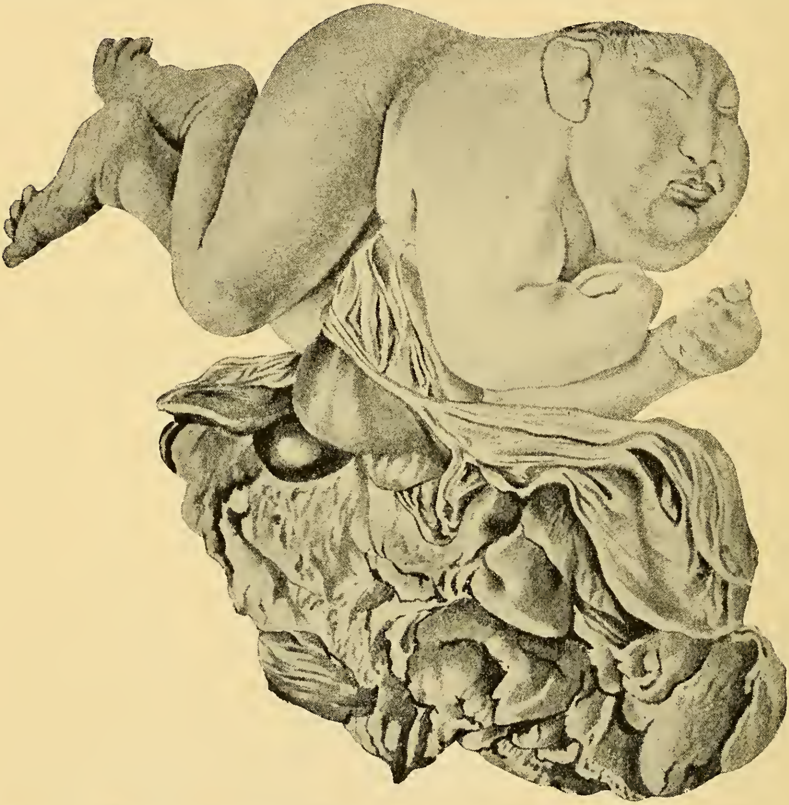

Fig. 27.—Case of Exomphalos, Anencephaly, and adhesion of amnion to umbilical aperture. Specimen No. 24.

retroflexion of the vertebral column (Fig. 28). The mother had given birth on previous occasions to four healthy children.

Another somewhat similar fœtus was given to me by Dr. C. B. Ker in 1894. The mother had previously had three children, all of them normal; during the present confinement she had suffered much from pain in the back and left iliac fossa unlike anything she had had in her former gestations. There was some hæmorrhage during the confinement, and the head, although descending easily on to the perineum, had to be delivered with forceps. The fœtus and placenta were born together. There was no excess of liquor amnii. The mother had never been strong, and the father was crippled with sciatica and was alcoholic. The fœtus, the sex of which was not apparent, had an exomphalic protrusion continuous with the mem-

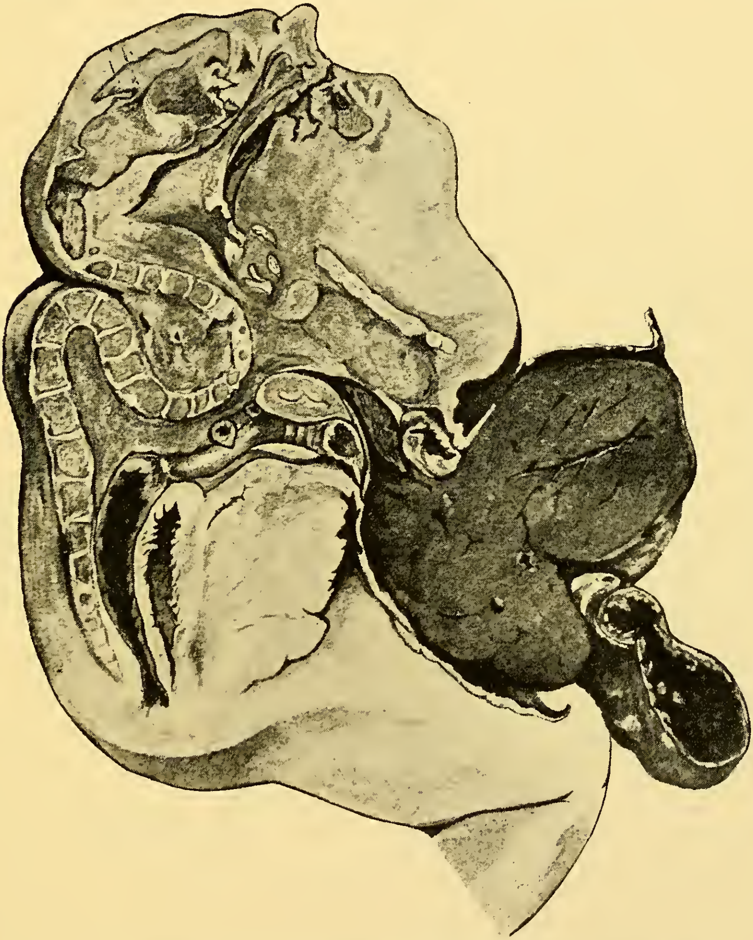

Fig. 28.—Frozen section of Specimen shown in Fig. 27, showing anencephaly, retroflexion of spine, and exomphalos.

branes and placenta; it had also a big sacral meningocele, clubbed feet, and an imperforate anus (Fig. 29). I exhibited the monstrosity to

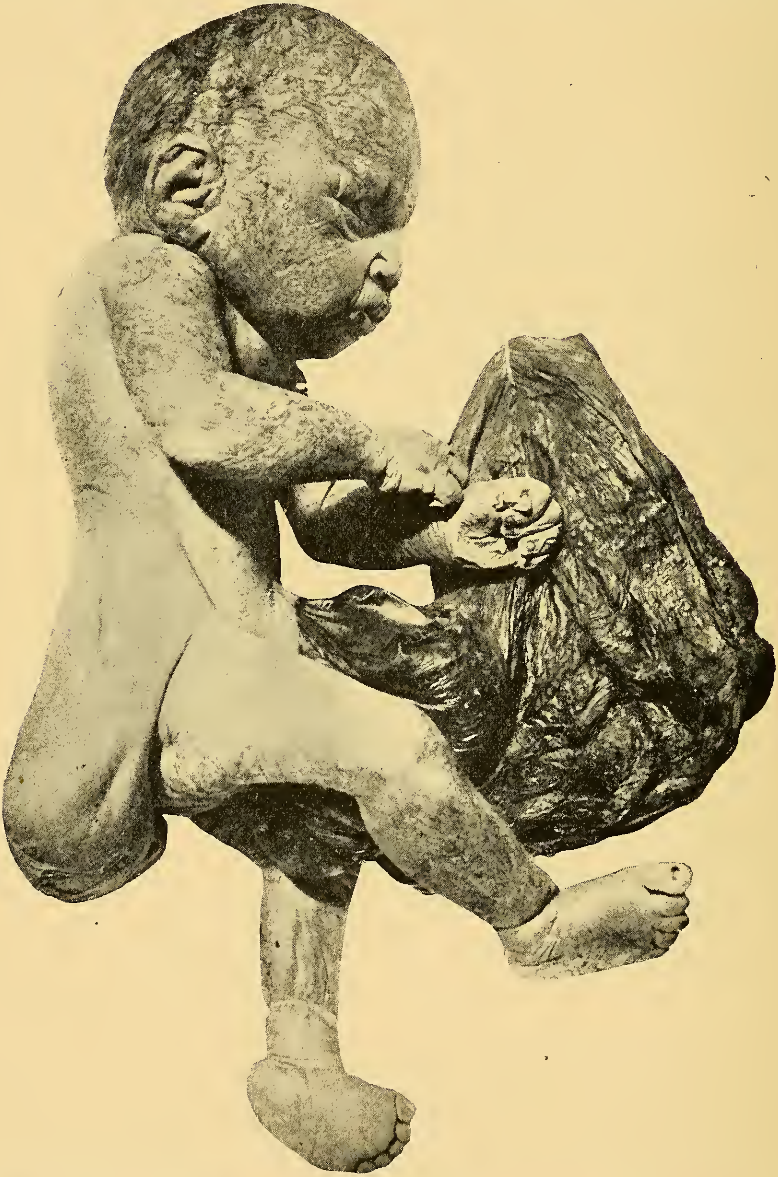

Fig. 29.—Fœtus showing exomphalos, the sac being continuous with the amnion, and sacral spina bifida. Specimen No. 124.

the Edinburgh Obstetrical Society (*Transactions*, vol. xix. 106, 1894). I have examined two or three other fœtuses in which the abdominal protrusion was almost certainly continuous with the amnion on the surface of the placenta; but as I did not obtain the afterbirth with the fœtus I shall not cite them as instances of amniotic adhesions.

Cases resembling more or less closely the above monstrosities have been put upon record in considerable numbers. Taruffi gathered together over forty of them (*Storia della teratologia*, i. 276, 1881; viii. 63, 1894), including one personal observation, and many others have been observed in the past ten years. Some of the authors of the articles in which these monstrosities are described may be named: they are Littré, Saxtorph, Breschet, Meckel, Heusinger, Rosenbaum, Hénot, Simpson, Otto, G. Braun, Calori, Gusserow, Dehn, Jensen, Johnson, Philipeaux, Oswald, Buschan, Leith Napier, Rischpler, and B. Marchese. In fact almost every writer who has reported a case of exomphalos has had something to say regarding the attachment of the amnion or of the placenta to the abdominal aperture.

The general characters of this type of monstrosity have been indicated in connection with the two cases that I have described. The chief character is the attachment of the placenta to the defective anterior abdominal wall of the fœtus by the instrumentality of the amnion, which, as a rule, passes from the margins of the opening to the surface of the placenta, leaving thus an enclosed space which contains the abdominal viscera. The viscera, therefore, come into contact with the chorion covering the placental surface at this point, as has been diagrammatically shown in connection with Leith Napier's specimen (*q.v.*). The umbilical vessels are not usually gathered together into a cord, but run on the inner aspect of the amnion to the placenta; they are consequently rather short. The intestinal coils may show adhesions to each other and to the amnion. Not uncommonly the defect in the abdominal wall extends low enough to affect the bladder (vesical exstrophy) and symphysis pubis; then the deformity has been called by the Germans *Bauchblasenschambeinspalte.* The vessels, especially the umbilical arteries and vein, are often anomalous. The genitals may be affected; there may be little or no indication of sex, or there may be a cloacal condition; the anus may be imperforate. The vertebral column is nearly always deformed (scoliosis), and the limbs may be clubbed or grooved or lacking in digits, or they may show dislocations. Some of the recorded cases have also had malformations of the head resembling those described in the first series of observations.

A *third* group of facts may now be referred to, namely those in which the amnion is attached to the back of the body of the fœtus. I have in my collection two fœtuses which show this amniotic anomaly. In one of them, which I got from Professor Simpson in 1889, there was well-marked exomphalos, a double facial fissure (Fig. 30), a cleft palate, a diaphragmatic hernia, a stunted condition of the right arm, irregularities of the digits, grooves round the limbs, a rudimentary penis, and an imperforate anus. In addition to these deformities, however, there was a curious conical projection near the lower end of the vertebral column, which seemed to contain the lower end of the spine in it, and from its tip a narrow band or filament passed round the right side of the fœtus to join the membrane (amnion?) in connection with the exomphalos (Fig. 31). During the pregnancy (seventh), or rather since the middle of it, the mother had suffered from pain in the left iliac and left lumbar regions, growing in intensity and becoming very severe during labour. The sac containing the abdominal viscera presented, and there was hæmorrhage during the confinement, calling for delivery by traction upon a foot. The placenta and membranes were not available for examination. My second case was that of a female anencephalic fœtus (Fig. 32) given to me by Dr. Lundie, and briefly described in the *Transactions of the Edinburgh Obstetrical Society* (vol. xx. 89, 1895). In addition to the anencephaly, there was talipes calcaneus, a malformed right thumb, and spina bifida in the lumbar region. From the margin of the spina bifida a band passed to the membranes, which were wrapped

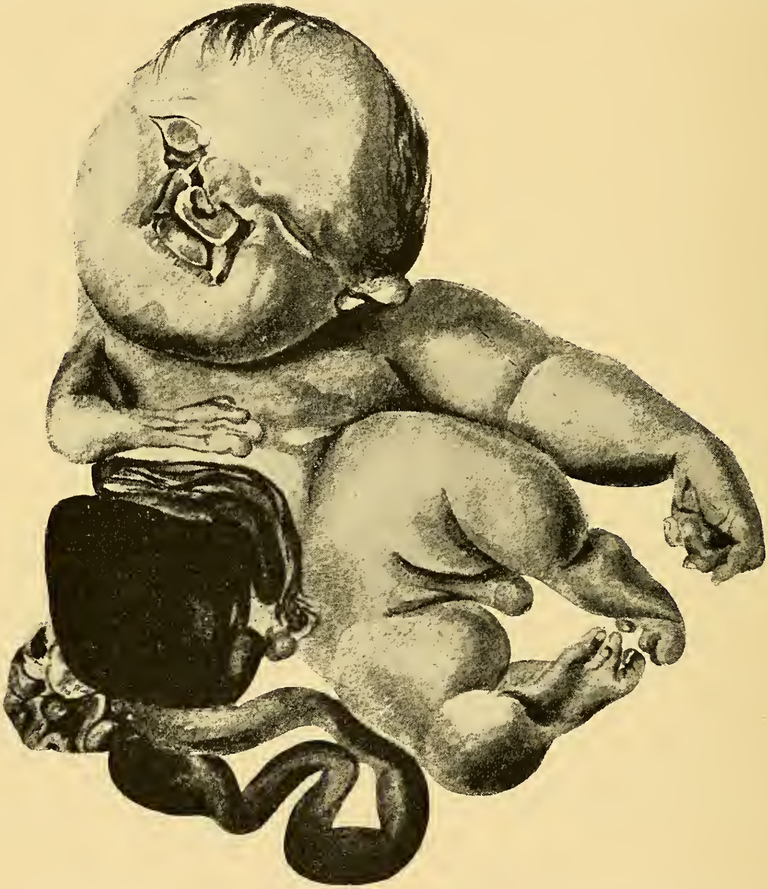

Fig. 30.—Fœtus showing exomphalos, facial fissures, and unilateral atrophy of right side. Specimen No. 23.

round the lower limbs when the specimen came into my possession (Fig. 33). The pregnancy had lasted eleven months; and the mother had already given birth to a hydrocephalic and otherwise malformed infant as the result of a former pregnancy.

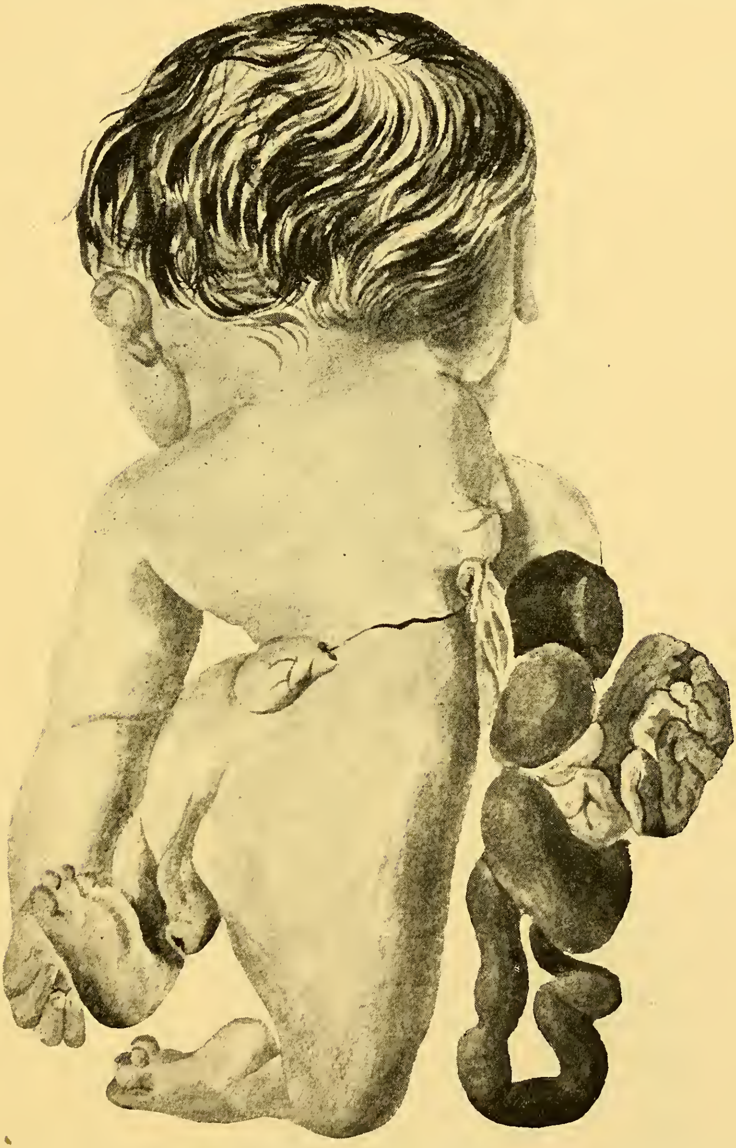

FIG. 31.—Posterior view of Fœtus (Specimen No. 23), showing sacral projection with band passing from it to exomphalic sac.

Cases such as the above would appear to be rare, but Strassmann

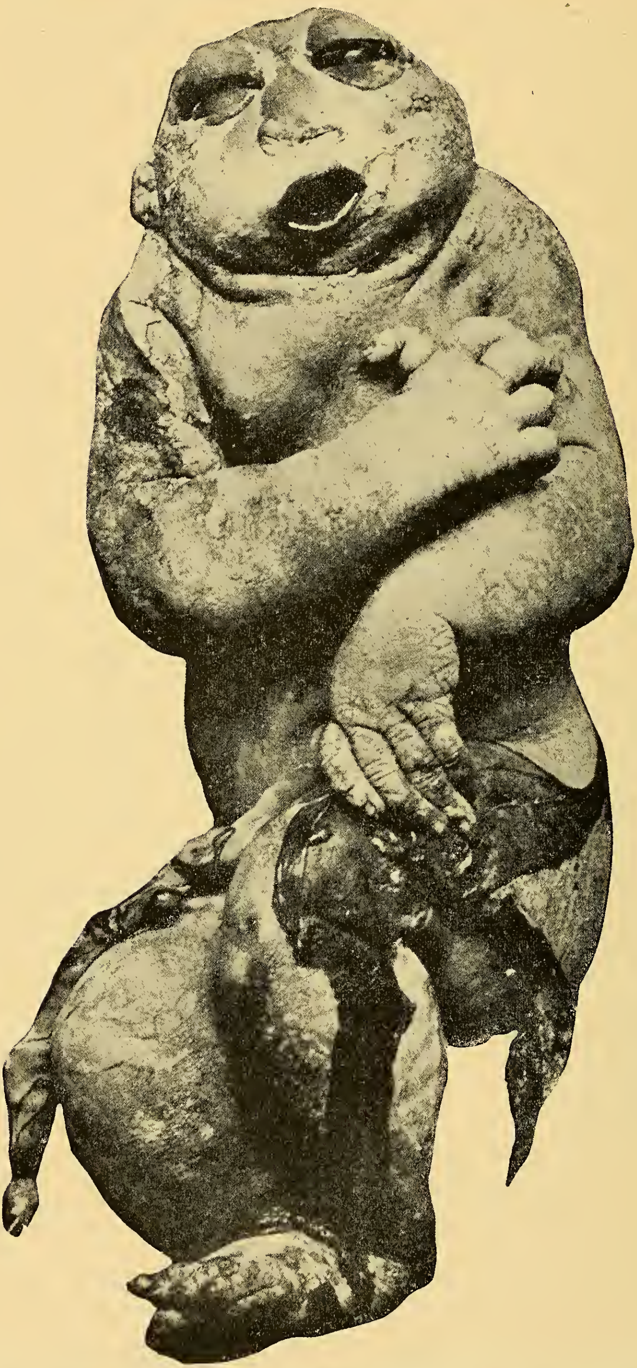

FIG. 32.—Fœtus with Anencephaly, Deformed Right Thumb, and Adherent Membranes. Specimen No. 148.

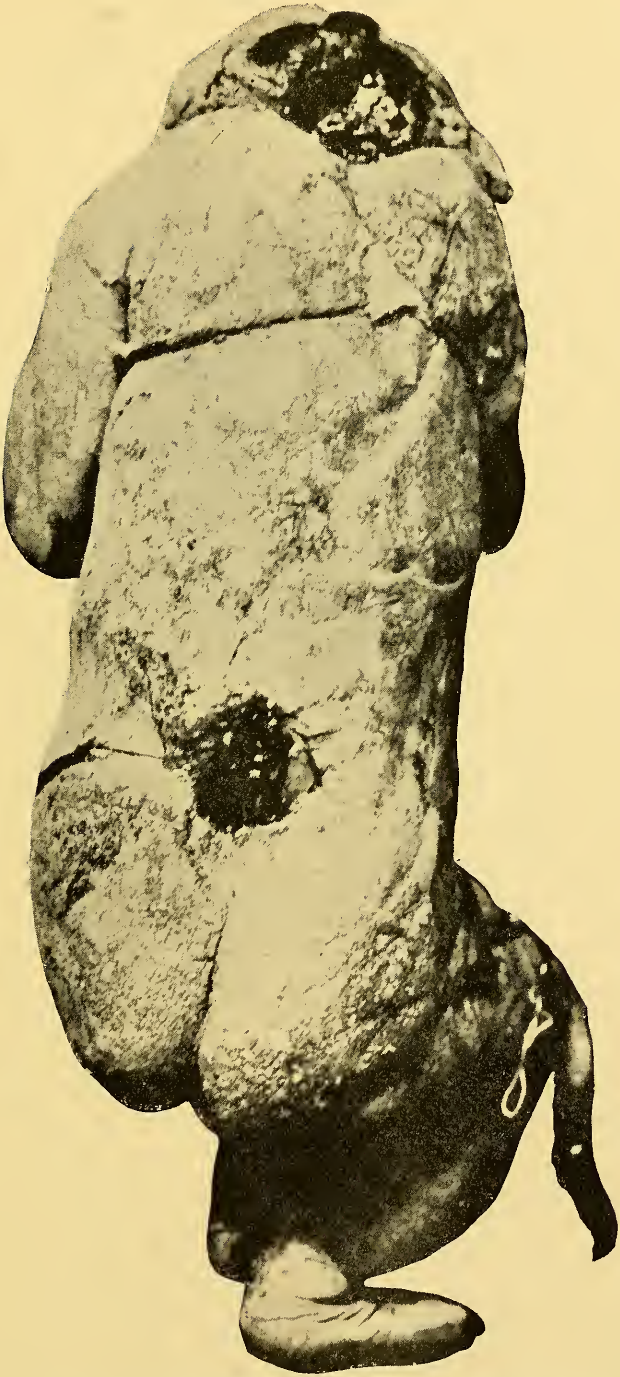

FIG. 33.—Posterior view of Fœtus (Specimen No. 148), with lumbar spina bifida and amniotic thread attached to it. Also shows anencephaly.

has described a specimen in which there was a spina bifida in the neck (spina bifida atlantica), and from its apex a band passed to the amnion. Ahlfeld, also, in 1894, figured a somewhat similar instance in which, however, the amnion was attached a little above the level of the neck; this case was apparently the one observed by Pinard and Varnier in 1892. There are, nevertheless, enough of such observations (*e.g.* those of Pies and Klotz) to prove that the amnion may be adherent to the back of the fœtus as well as to its head and to the anterior aspect of its abdomen.

In a *fourth* detachment of the facts which I am attempting in some sort to classify and marshal are the cases in which the adhesion is between some part of the fœtus and the umbilical cord, or rather the covering of the cord. I have not myself met with an example of this variety of amniotic adhesion, but many such have been reported by careful observers, so that Taruffi (*Storia della teratologia*, i. 280, 1881; v. 303, 1889; viii. 66, 1894) was able to collect more than twelve of them, including those by Portal, Burggrav, Sandifort, Walter, Meckel, Nicati, Haan, Simpson, Tessier, Klotz, Hein, Hager, Garnett, and Leopold. Within recent years several interesting cases have been added to the list, and I may specially refer to those of F. von Winckel and of Couvelaire. In the former an amnio-amniotic band arose by a broad basis of attachment from the placenta near to the origin of the umbilical cord, and formed a figure of 8 loop round the cord and round the right upper arm of the fœtus; a distinct circular groove was thus produced in the arm; a torn band was also found attached to the index finger of the left hand. In Couvelaire's specimen the fœtus had died suddenly during labour; it was a male and was not malformed. The placenta was circular; the membranous sac was incomplete, the half only of the placental border giving attachment to a large membranous piece, which included the amnion, chorion, and decidua. From one border of this piece a thin strip, formed by amnion, passed to the umbilical cord around which it was coiled three times and knotted as well; then it passed on to a separate piece consisting of chorion, amnion, and decidua. The umbilical cord was 51 cms. long, and was very thick and œdematous save at the point of constriction, where its diameter was only 7 mms. The amniotic or inter-amniotic band was more than 23 cms. in length. In the cases of F. von Winckel and Couvelaire the fœtus was not specially malformed, but in some of the other reported instances (*e.g.* Haan's) it was clearly monstrous.

A *fifth* group contains the cases in which a band has been observed passing from one part of the fœtus to another or from one part of the amniotic covering of the placenta to another. I have, in my collection, three well-marked instances of this type of malformation. In one of them, a fœtus with placenta which I received from Dr. Maclagan, of Sleaford, Lincolnshire, in October 1901, there was marked exomphalos, and the right arm was fixed to the margin of the aperture in the abdominal wall by a band of skin inserted into the wrist (Fig. 34). The mother had always been very

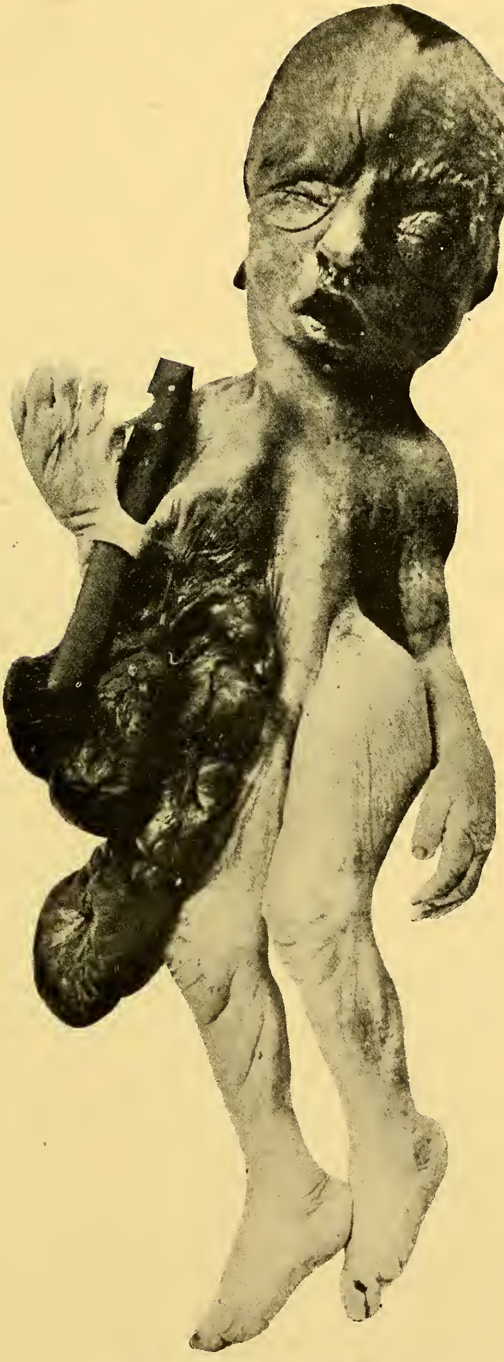

Fig. 34.—Fœtus with Exomphalos and Cutaneous Band from wrist to margin of opening in abdomino-thoracic wall. Specimen No. 268.

delicate and subject to fainting fits; this fœtus was the product of her second pregnancy. Another specimen illustrating the adhesion of different parts of the fœtus to each other was that of a small twin born along with a normal infant; there was a single placenta, by far the larger part of which belonged to the normal infant; the small fœtus had its own amniotic sac, and showed membranous union of the lower limbs with partial rotation of them, so that the right heel looked forwards (Fig. 35). The membrane between the legs seemed to be continuous with the sheath of the umbilical cord. It is probable that there was here the first stage of sympodia, and that the membranous adhesion had to do with its origin. The mother was healthy, but had had two miscarriages as well as five earlier normal labours. The specimen was given to me by Dr. Lundie in 1898. The third specimen to which I shall here refer has been mentioned already; it was the case of exomphalos, facial fissure, and adhesion of the amnion to the head sent to me by Dr. Richards, of

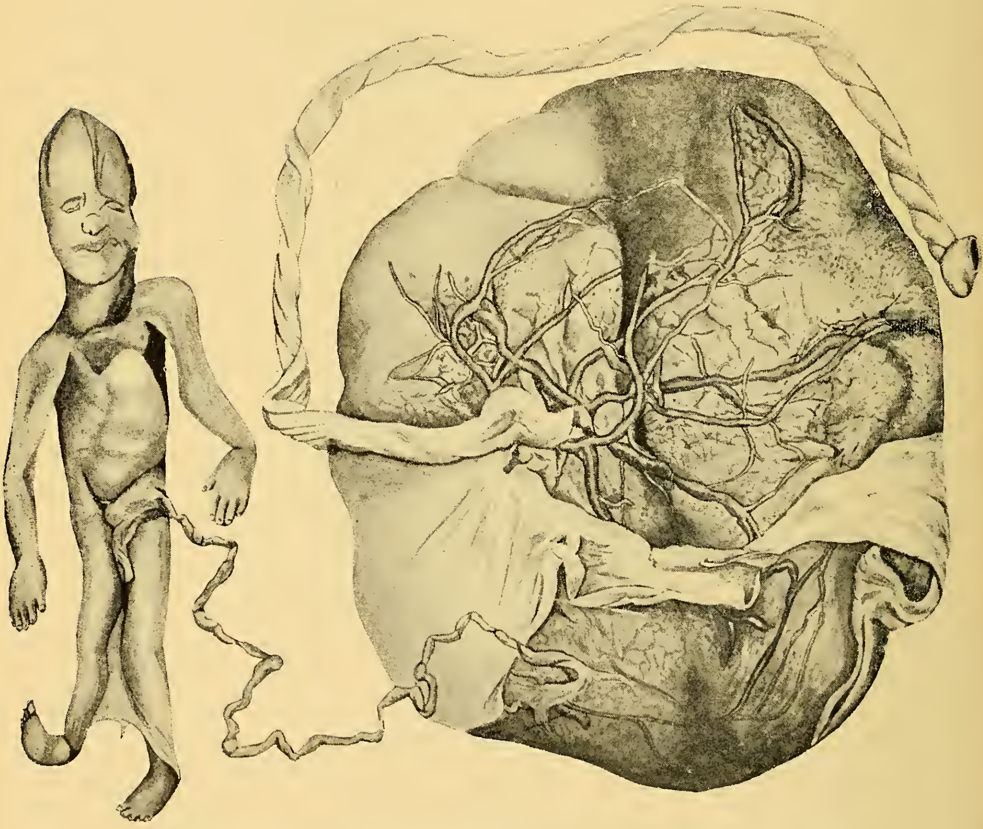

Fig. 35.—Twin Fœtus, showing early stage of sympodia and fused placenta. Specimen No. 209.

North Ormesby (Fig. 25); and in addition to the above deformities the fœtal aspect of the placenta showed a filiform band (amniotic) fixed to it at both ends and forming a loop; probably some part of the fœtus had lain in this loop during intrauterine life, but there was nothing to indicate what part it had been.

Several cases illustrating the above type of adhesion are to be found in the literature of the subject. The first of the two fœtuses described by C. L. Klotz, for instance, is a good example; in it the amniotic surface of the placenta was adherent to the back of the infant, there was an amniotic adhesion to the face, and in addition there was a cutaneous bridge in the lower part of the back. These adhesions of bands may be called fœto-fœtal or amnio-amniotic, according as they pass between two parts of the fœtus or of the amnion. Possibly the weblike structure (*Flughautbildung* of the Germans) which is in rare cases found passing between various parts of the body may be of the same nature as the fœto-fœtal bands referred to above. The weblike expansion, to which the name *patagium* may be conveniently given, may pass from the neck to the shoulder on one or both sides, as in O. Kobylinski's observation (*Arch. f. Anthrop.*, xiv. 343, 1883); or it may stretch from the posterior aspect of the thigh to the back of the leg, as in the cases of J. Wolff (*Arch. f. klin. Chir.*, xxxviii. 66, 1889) and K. Basch (*Ztschr. f. Heilk.*, xii. 499, 1891; *Prag. med. Wchnschr.*, xvii. 289, 1892); or it may reach like a wing from the upper arm to the chest-wall, as in the instances reported by L. Bruns and L. Kredel (*Fortschr. d. Med.*, viii. 1, 1890), by J. Benario (*Berlin. klin. Wchnschr.*, xxvii. 225, 1890), by J. Thomson (*Teratologia*, ii. 1, 1895), and others. The *patagium* may not be amniotic in origin, but it is sometimes found associated with malformations which are generally regarded as such.

A *sixth* group of facts concerning this complicated and perplexing amniotic problem contains the observations which have been made upon the relation of bands of the amnion to malformations of the limbs. The number of cases in which deformities of the extremities of almost all kinds have been ascribed to the action of the amnion is very large; but the instances in which bands or filaments or adhesions have been actually recognised are comparatively few. Of course only the cases in the latter category can be looked upon as facts in the strict sense of the word. To this sixth group of facts belong the so-called spontaneous or intrauterine amputations; to these interesting deformities I have already alluded in the first part of this Manual (p. 396), and also in the preceding chapter in connection with the possible teratogenic influence of the umbilical cord. I need not, therefore, repeat here what has been previously stated regarding them.

The deformities of the limbs which have been ascribed to amniotic bands and filaments are very various, and in only a few of them have the connections with the amnion been actually found in situ. I have not myself had an opportunity of examining a case in which the bands were to be seen attached to the deformed part of the limb, but others have observed this, and there is no reason to doubt its occurrence; probably the process of birth is a great means of tearing and separating these connections. F. von Winckel was fortunate in being able to record and figure a case in which an amniotic band arose from the placental surface by a broad basis, passed to encircle the left upper limb, then formed a loop round the umbilical cord, and finally returned to the placenta; in its course it made a figure of 8 convolution; there was marked smallness of the limb above the constriction; and there was a second short band attached to the index finger of the left hand, which doubtless represented a torn-across filament. J. Wolff's observation (Fig. 36) was even more demonstrative of the direct connection between the deformity of an extremity and an amniotic band: in it a stout thread to͂ok origin from the fœtal surface of the placenta, and passed to the tip of the middle finger of the right hand of the fœtus, the nail of which was deformed; it then was continued to be attached to the ring finger, the terminal phalanx of which was fixed to the hand only by a thin band; the whole length of the band was 10 cms.; the left hand showed syndactyly of the ring and middle fingers, and their terminal phalanges showed constrictions and defects, which Wolff regarded as probably due to a second amniotic band which had disappeared.

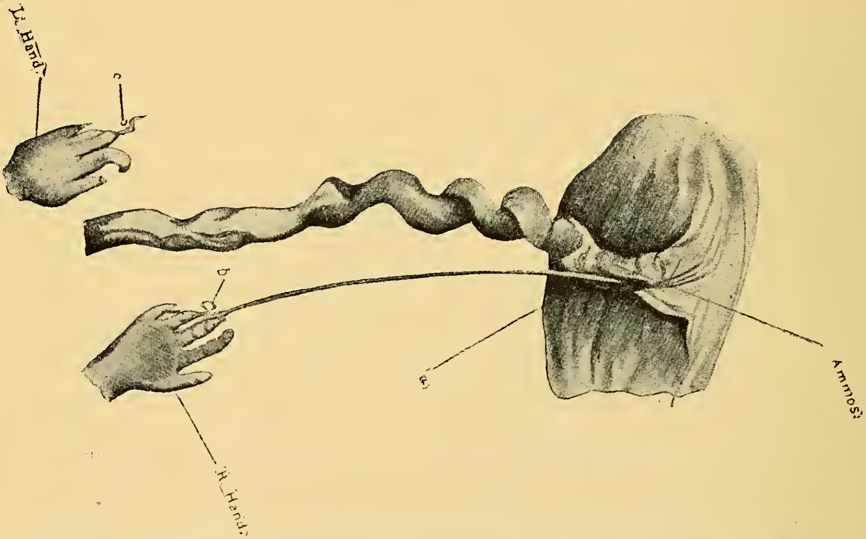

Fig. 36.—J. Wolff's case of Amniotic Adhesions to the Fingers (*vide Arch. f. Gynaek.*, lx. 281, 1900).

In other cases, malformations of the extremities are present and amniotic bands are present, but the two are not connected together; in such instances, therefore, the evidence of structural continuity between the bands and the deformities (grooves, amputations, contortions) is not flawless, but it is strong enough to merit a general acceptance. In Moreau's case, for instance, the fœtus showed amputations of several digits, and the amniotic surface of the placenta showed threadlike bands, some of which hung free at one end while others were attached at both ends. It is reasonable to connect together the two abnormal states. In yet other cases various malformations of the extremities are to be noted, and bands may be found adhering to them; but there are either no traces of anomalies of the amnion, or, what is more common, no information is forthcoming about the amnion, for the sufficient reason that it has not been preserved or examined at the time of birth. Many examples of these imperfectly observed and recorded cases are to be met with in obstetrical literature, and to some of them I must now direct the reader's attention. I may add that I have had occasion in my own experience twice to lament the loss of such specimens: in one instance through my absence from Edinburgh on University work in Aberdeen I missed seeing a case of multiform deformities of the digits of a premature infant, and I lost the chance of securing the membranes if not also the fœtus for examination; in the other instance a medical friend told me of the birth in his practice of an infant whose fingers showed all the stages of intrauterine amputations, one of them having a raw surface at the tip; in this case also no post-mortem examination was allowed, and the placenta and membranes were not secured for inspection.

Perhaps the most interesting of all these imperfectly recorded cases are the two referred to by J. U. T. Schaeffer in 1775 (*vide* Bibliography at the end of Chapter X.) and by P. Zagorsky in 1834. Unfortunately I have not been able to consult these records in the original. The following notes of them, however, are given by J. Y. Simpson in his article published in 1836. In Schaeffer's specimen the fingers of the right hand showed syndactyly, and the thumb was large and without a nail; the thumb of the left hand also had no nail, and the index and middle fingers wanted their second and third phalanges; the second toe of the right foot had a sort of membranous cord attached to it, and the great toe was short, deformed, and had a cicatrix where the nail ought to have been; all the left leg below the gastrocnemii seemed, as it were, absent, and from the uncicatrised central part of the stump a fibrous cord took its origin, to which was appended a small body which "on minute examination proved to be a foot of the size of one belonging to a fœtus of the third month, with divisions on its inferior edge representing the five toes" (Fig. 23). The infant was at the eighth month. Zagorsky's specimen was a five months' male fœtus: the head and face were deformed, in much the same manner as in the cases of amniotic adhesion to the head to which I have referred (*vide* p. 169); the right hand was slightly malformed, and the left hand greatly so, the fingers being absent or represented only by cutaneous nodules; the right thigh ended in a rounded stump, from the centre of which a slender, threadlike membrane ran across to below the middle of the left leg, which it encircled, causing a groove; from about the middle of the threadlike membrane joining the two legs, a small oblong body was suspended, which on inspection proved to be the right foot, of the size of the foot of a fœtus of the tenth or twelfth week. The importance of these two cases can hardly be exaggerated; for, if they were accurately described and figured, they prove almost to demonstration that threadlike bands can lead to the amputation of fœtal parts. J. Y. Simpson, however, refers to the defective representation of the structures in Zagorsky's original drawing; and it is a striking fact that no such clearly teratogenic bands (with the possible exception of the case reported by Fieux) have been recognised in recently published observations. While, then, we must regard Schaeffer's and Zagorsky's cases as facts, it is perhaps not so certain that the little filipendulous foot represented in the accompanying illustrations was also an indubitable fact. Besides the cases of Schaeffer and Zagorsky, instances of deformed limbs with bands adhering to them have been put on record by Montgomery (1837), Frickhoeffer (1856), Credé (1858, 1869), Barkow (1859), Kottmeier (1864), Reuss (1869), Fürst (1871), and many others. In the recent case of Fieux (1902) there was a filipendulous hand instead of a foot (" une petite main en miniature ").

Finally, in this sixth detachment of facts must be placed the cases in which malformations of the limbs have been met with, which, although no traces of bands or amniotic connections have been discovered, have yet been ascribed to such agencies simply because they have resembled the malformations in which amniotic adhesions were present. I have seen several instances of this kind. In 1891, for example, I saw, with Dr. T. B. Darling, a baby of a few days old whose right arm looked as if it had been amputated at the wrist (Fig. 37); there was a well-formed conical stump with five little nodules at the end of it which Dr. Darling regarded as rudimentary fingers. The child was otherwise well formed, and no convolutions of the cord or bands from the amnion had been observed at birth. This case was shown to the Edinburgh Obstetrical Society in March 1891 (*Transactions*, xvi. 89, 1891). In 1898, I had the opportunity of examining Dr. Gemmill Thomson's case of an armless male infant; the arms looked as if they had been amputated at the shoulder, and the lower limbs were stunted; the child was shown at a meeting of the Glasgow Obstetrical Society (*Transactions*, i. 73, 1898), and its anatomy was described by Dr. Lindsay in 1899 (*Transactions*, ii. 16, 1901). In 1900, I published (*Interstate Med. Journ.*, vii. 367, 1900) an account of a kitten born without the right forelimb; the specimen had been given to me for examination by Dr. J. K. Drysdale. Cases, like these which I have met with, have been reported in large numbers in medical literature; and, on account of the dexterity which armless individuals have gained in using their feet instead of their hands, the subjects of these deformities have forced themselves upon the attention of the general public as well as upon that of the teratologist. Connecting links between the so-called spontaneous amputations and the normal are found in the cases in which there exists a more or less circular and a more or less deep groove round an arm, a leg, or a digit. F. Potier, for instance, reported a case in 1898 in which an infant, born at term, showed radial paralysis of the right arm; on the external surface of the limb at the point where the radial nerve traverses the humeral groove there was an irregular rather deep depression of the skin, regarded by the writer as a sort of cicatrix attributable to the pressure of an amniotic band; the histological examination of the skin of the affected area showed an increase in thickness and density of the dermis, a thickening of the rete Malpighii, and a marked development of sebaceous and sudoriparous glands; the radial nerve was found to exhibit an increase in its connective tissue elements, and changes in its nerve elements consisting in disappearance of nuclei and axis-cylinders and retention of vestiges only of myeline; the affected muscles had fibres smaller than normal and less distinctly striated. Potier's record differs from most of the others that are to be found in literature, in the fact that the histological characters of the skin and underlying structures at the site of the groove are described; too often these important details are lacking.

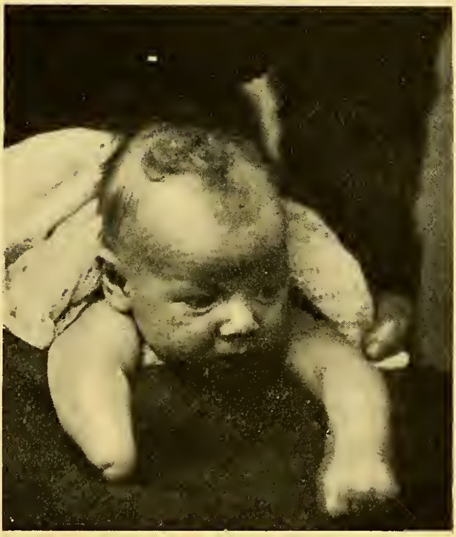

Fig. 37.—Infant with Spontaneous Amputation of Right Hand. Case No. 41.

A *seventh* detachment of facts regarding the amniotic theory must now be drawn up in orderly array before the reader; if indeed that sorely tried individual has not already grown wearied of the whole subject and turned his attention to some other part of this volume. Several cases have been observed, and the number is constantly being added to, in which there is good evidence to show that the fœtus, if not the embryo, has developed outside the amniotic cavity. Both Hamard and Osmont have described a case of this kind which occurred in the hospital practice of Dr. Paul Bar; Bar also put on record a second somewhat similar case; other instances are those of Lebedeff (1878), of Maygrier (*L'Obstétrique*, iv. 303, 1899), of M. V. Cathala

(*L'Obstétrique*, vii. 309, 1902), and of Perret (*L'Obstétrique*, vii. 316, 1902); and E. Glaize dealt with the whole subject of *La grossesse extra-membraneuse* in a *Paris Thèsis* in 1899. In Bar's specimen the chorion contained a fœtus which lay free in it; the amnion consisted of a small sac from which the root of the umbilical cord emerged; and attached to the outer surface of the amnion were several threadlike bands or amniotic fringes. The fœtus showed malformations of the nature of grooves round the left leg, the toes, and the fingers; there was also syndactyly, some of the digits were defective in the number of the phalanges which they contained, and to the left hand a membranous band was attached. Crouzat and Payrau (*L'Obstétrique*, vi. 235, 1901) met with a case of twin pregnancy in which the first-born infant was normal; the second fœtus had exencephaly and various facial and digital malformations (fissures, grooves, adherent bands), was attached to the afterbirth by a very short cord (about 4 inches in length) and by two broad membranous bands, and had been expelled from its proper amniotic sac and acquired adhesions with the chorion. The fœtus in the second case reported by Bar also showed congenital grooves on the digits; but these malformations are not constantly associated with an extra-membranous fœtus, for in Cathala's five months' specimen there were no deformities at all, neither were there any in Dubrisay's case exhibited at the meeting of the Paris Obstetrical Society in March 1901 (*L'Obstétrique*, vi. 274, 1901). Further, in a very curious specimen met with by Tarnier (1896), as well as in one somewhat resembling it described by Bar (1898), the fœtus must have developed outside both the chorion and the amnion, between these membranes and the uterine wall; yet in these two instances the fœtus was not malformed. The observations of C. Giacomini on emigration of the human embryo in early abortion sacs (*Sulle anomalie di sviluppo dell' embrione umano*, Torino, 1895) are similar to the cases which have been met with by Bar and others at a later date in pregnancy; in some of Giacomini's specimens the embryo had wandered into the outer cœlomic cavity and in others it had passed through all the ovular membranes. H. Knoop's 2 mm. embryo was attached by its back to the chorion (*Beitr. z. Geburtsh. u. Gynaek.*, vii. 284, 1903). These extra-amniotic and extra-membranous fœtuses form an interesting group of facts which must in the future find a place in all theories of amniotic influence in teratogenesis.

An *eighth* and final series of facts contains the observations which have been made upon amniotic bands, adhesions, and pressure in the lower animals. Apparently, amniotic adhesions are very rare in Comparative Pathology, for Taruffi (*Storia della teratologia*, i. 283, 1881; v. 301, 1889) has only been able to find three cases, two of which were reported by Gurlt (*Ueber thierische Missgeburten*, plate ix. fig. 57; plate xiv. fig. 75, Berlin, 1877), and one by Millot (*Journ. de méd. vétér.*, v. 53, 1834). One of Gurlt's specimens was a lamb with a wide buccal aperture (megalostomus) and the amnion adherent to a hydrocephalic sac; the other was a calf-fœtus with cyclops, megalostomus, and the membranous amnion attached to a hydrencephalocele. Millot's specimen was also a calf, and the amnion was fixed to the left cheek below the eye. In strong contrast with the scarcity of observations of amniotic adhesions in the lower animals is the large number of cases in which it has been found possible artificially to arrest the development of the amnion in the hen's egg during incubation. C. Dareste, in his long, laborious, and epoch-making series of experiments upon the chick during development (*Production artificielle des monstruosités*, Paris, 1877; 2nd edit., 1891), was early struck by the frequency of the coexistence of various malformations and monstrosities with arrested development of the amnion. Sometimes, although rarely, the amnion was not developed at all, and then the embryo usually died early or was more or less gravely altered in its form; more commonly certain parts of the amnion, *e.g.* the cephalic or caudal folds, were delayed in their evolution, and then the embryo was monstrous in the part corresponding to the defect of development of the surrounding membrane. Dareste ascribed these embryonic defects to pressure produced by the non-separation of the amnion from the body or head of the embryo, and believed that in this way it was possible to account for most of the simple monstrosities, such as anencephaly, cyclopia, and sympodia, and for many other malformations.

Such, then, are some of the facts connected with this great amniotic theory of teratogenesis. I have endeavoured to pass them before the reader's mental vision in some sort of regular order; I have tried to show that after all there is a certain, if obscure, arrangement of them, and that they are not unrelated to one another. I have enumerated illustrative cases in which the amnion has been found at birth to be adherent to the head, face, abdomen, back, and limbs of the fœtus; I have referred to instances in which amniotic bands have been seen stretching from one part of the general amniotic surface to another, and to others in which cutaneous bands have passed from one part of the fœtus to another; I have cited examples of so-called spontaneous amputations, in some at least of which amniotic bands seemed undoubtedly to have been instrumental in their production; the curious cases have been alluded to in which the fœtus seems to have developed entirely outside the amnion if not also outside the chorion; and reference has been made to defects in the amnion discovered in association with experimentally induced monstrosities in the chick. The survey has been a long one, for the field of facts has been a large one; but an apology is hardly called for, facts of all kinds being of no little value and the time expended in mastering them being well spent. Facts are indeed the data of experience and observation and have a prime importance; factlessness is a quality most fatal to a subject appealing to the scientific mind, as we trust Antenatal Pathology does appeal; but we must not be content with the accumulation of facts, we must pass sooner or later (the fashion of the day is later rather than sooner) to contemplation of the facts, to reflection upon them, and to the drawing of conclusions from them. What do the facts mean? What can we learn from them? Have they anything to teach us? Thus are we brought naturally enough to the second part of the amniotic theory, to the reflections based upon the facts, to the interpretation of the phenomena, to the thinker's thoughts about the observer's data. The data are the things given to us, not simply to be labelled, catalogued, and placed safely on the shelf, but to be absorbed, intellectually assimilated, and given back again to Science in the form of conclusions, inferences, deductions, and theories. Let us now consider the theories or hypotheses that have grown up around the facts.

Etienne Geoffroy Saint-Hilaire (*Philosophie anatomique,* pp. 237, 530, 539, 1822) was glad to seize upon the notion of adhesions to the amnion as a reasonable and sufficient cause for the various monstrosities which he had met with. At first, he wrote, the spectacle of monstrosities so numerous and so extravagantly bizarre led him to think of the constructive forces in their saturnalian days ("dans ses jours de saturnales"), tired out with the weary task of formation and seeking relaxation in capricious developments. To him amniotic adhesions offered a scientific explanation of what had seemed inexplicable, fantastic, a saturnalia of bizarrerie. He saw in bands passing from the membranes to the fœtus the single and satisfactory explanation of all monstrosities. The fœtus was like the lung in the pleural sac; its skin, if not surrounded by liquor amnii, might contract adhesions with the enveloping membranes; these adhesions were vascular in their nature; and the viscera of the fœtus, if not shut off from the exterior, might become attached by such vascular connections to the placenta. "Je crois," he wrote, "qu'il n'est qu'une cause unique, générale et extérieure de monstruosités, qu'il n'existe qu'un seul mode pour faire dévier les formations organiques de l'ordre commun; c'est quand le fœtus contracte des adhérences avec ses membranes ambiantes." Meckel, however, thought that Saint-Hilaire's explanation could only hold good in a few cases, for in all his specimens there had been no adhesions. C. E. Rudolph, in 1829, went a step further and maintained that the adhesions were not the cause but the effects of the monstrosity of the fœtus. He was of opinion that if the fœtus were brought near to the placenta it might compress and irritate it and so lead to adhesions; or that, if the skin of the unborn infant were the seat of inflammation, a plastic lymph might be thrown out which would form adhesive bands glueing it to the membranes. He thought also that if the fœtus had the monstrosity known as anencephaly, pointing to antecedent hydrocephalus (*i.e.* inflammation of the brain), the inflammatory changes would occur with all the greater probability.

Isidore Geoffroy Saint-Hilaire, influenced perhaps by the criticisms to which his father's theory had been subjected, stated that he did not regard it as applicable to all monstrosities and anomalies, but only to those characterised by defect, by displacement, and by want of union of contiguous surfaces; when no adhesions were to be seen he supposed that they had been torn through (*Histoire des anomalies,* iii. 523, 1836). While, however, these criticisms and their consequences were in process of elaboration on the Continent, Montgomery and J. Y. Simpson were engaged in the study of what may be called the finer varieties of adhesions and bands. The Saint-Hilaires had dealt only with the gross lesions due to widespread union between the fœtus and the amnion covering the placenta; but Montgomery got the help of a newly observed series of facts, the cases in which the limbs are surrounded by threadlike ligatures and show various stages in the production of amputations and other malformations. In 1832 Montgomery wrote of these ligatures as "distinct threads of, I presume, organised lymph," and explained their mode of action as follows: "From the condition of the limbs thus produced, and the impossibility of the parts below the ligatures continuing their growth under such circumstances, it seems exceedingly probable that, as the child continued to live and grow, the parts of the legs below the ligatures would have been separated and thus undergone spontaneous amputation; the formation of these threads, and particularly their application so as to stricture the limbs, are circumstances in explanation of which I do not feel prepared even to hazard a conjecture." J. Y. Simpson accepted Montgomery's view that the bands were of the nature of organised lymph; he proceeded to expand the theory in the following words: "That this lymph has been effused by inflammatory action is, I am inclined to think, in the highest degree probable. No one would now attribute such morbid bands or cords, if they were found in other parts of the body, as in the cavities of the chest or abdomen, to any other morbid action than that of inflammation; and that the cutaneous texture of the fœtus in utero is liable to inflammation attended with the effusion of organisable lymph is known from the circumstance of different parts of the surface of the fœtus being occasionally found adhering, either directly or by the medium of false membranes, to the amnion covering the placenta, . . . to some part of the umbilical cord, . . . or to other parts of its own body. Further, that organisable lymph, when effused by inflammatory action between two contiguous parts of the surface of the fœtus, is capable of being changed into pseudo-membranous bands or cords, similar to those observed in Dr. Montgomery's first case, and in the cases described by Schaeffer and Zagorsky, appears from the circumstance of lymph occasionally assuming this form, when effused between the contiguous points of such surfaces as have a free motion on one another, as is sometimes seen in the bands of false membrane found stretching from one point to another of the cavities of the pleura, pericardium, and peritoneum." It is quite clear, from these quotations, that Simpson regarded Montgomery's bands as similar to those found in cases of pleuritis and peritonitis, and as due to an inflamed condition of the two apposed surfaces of the fœtal skin and the amniotic membrane during intrauterine life. Here, then, was the theory of disease of the amnion as the cause of monstrosities stated fully and freely; and other writers were not slow in applying it to the explanation of many other deformities besides those specially considered by Montgomery and Simpson.

The amniotic theory, in its strictly nosological aspect, met with a good deal of criticism. Simonart (1846), while generally accepting the conclusions reached by Simpson, gave to the bands the unfortunate name of "ligaments," and did not exclude the possibility of the adhesions being due to cutaneous ulcers. Kristeller, in 1859, also admitted the existence of inflammation of the skin. Scanzoni, from a consideration of the anatomical characters of the amnion, doubted whether it could produce an inflammatory exudation, and was inclined to think that the lymph transuded through the membrane from the wall of the uterus. Houel was rather inclined to adduce shortness of the umbilical cord as an important causal agent; it kept the fœtus in close contact with the membranes, and so favoured adhesion; but he did not take into account or explain the instances in which the cord had been found of usual length. G. Braun advanced again the statement which Etienne G. Saint-Hilaire had originally made, that the liquor amnii must be scanty to permit of the formation of adhesions; when it is small in amount the amniotic membrane (or folds of it) remain in contact with the fœtus; these folds are with growth drawn out into bands, and by the traction they exert upon the fœtal parts lead to malformations of them. The coexistence of hydramnios (instead of scarcity of the amniotic fluid) with monstrous conditions of the fœtus was a difficulty in the way of the acceptance of this theory, and no very satisfactory solution was forthcoming. Thus several arguments were brought forward against the nosological theory of amniotic influence in teratogenesis. To these must be added the fact that the bands had been found to consist sometimes at least of amnion and not of organised lymph, and the circumstance that while such diseased states of the amnion might account for malformations and monstrosities by defect, they could in no degree explain the monstrosities by excess and the double terata.

About the middle of the nineteenth century a new factor came into the consideration of the amniotic theory in teratogenesis: Embryology by its discoveries began to throw light upon the nature and mode of origin of all the fœtal membranes and vesicles, including, of course, the amnion. The thoughts of teratologists were thus turned into a new channel, and this new channel led the current of the theory rather away from than towards the nosological side of it. As a matter of fact, the intrusion of the embryological factor distinctly weakened the hypothesis of disease of the fœtal membranes as a cause of deformity and monstrosity. As soon as it began to be recognised that the amnion, in some of the lower animals at least, was formed by the upgrowth of folds of the epiblast and mesoblast of the blastodermic vesicle extending until they met all round the embryo and walled it in, just so soon it began to be apparent that any arrest in the development of these folds or any deviation from the normal mode of their upgrowth would lead to the establishment of abnormal relations between them and the embryo lying within them. For a time the attempt continued to be made by some writers to reconcile this developmental defect with the notion of disease either of the amnion or of the fœtus. The idea that commended itself seems to have been that an inflammatory irritation of the amnion or of the embryonic parts opposed to it served to prevent the regular and complete separation of the two structures; liquor amnii would, however, be poured out at certain places, and so an imperfect and irregular separation would occur and the unseparated parts would remain as bands or adhesions or filaments. Calori and G. Braun apparently held views of this nature, and Jensen (in 1866) expanded them by emphasising the fact that the amnion was developed in several folds (cephalic, caudal, lateral); and that, as one or other of these parts was affected, so the resulting deformity or monstrosity would vary in its position and character. Perls (*Lehrb. d. allg. Pathologie*, ii. 255, 1879) also gave a pathological or nosological bearing to the theory, by supposing that substances passing from the mother to the fœtus might cause irritation of the parts and especially of the amnion in their transit, and so set up localised inflammation and the formation of bands and adhesions. In some instances, he thought that mechanical compression also might cause inflammation.

Gradually, however, the nosological idea was allowed to drop out of the amniotic theory of teratogenesis, and this change was largely due to the results of the experimental production of monstrosities in the case of the chick. Panum, Lombardini, and more particularly Dareste have shown that by altering the environmental conditions during the incubation of the egg—by varnishing the shell, by raising or lowering the temperature in the incubator, by shaking the incubating tray, etc.—we can produce malformations, monstrosities, or defective developments in the embryo, although we can never foretell which particular anomaly will be presented. Dareste found that in most of these cases it was the development of the amnion that was at fault, that there was usually a defective secretion of liquor amnii in the amniotic cavity; and that, in consequence thereof, the membrane remained in contact with the surface of the embryo and exercised pressure upon it. The reader will notice, therefore, that the effect of embryological investigations and of experimental teratogenesis has been to resuscitate the pressure-theory. When the amnion does not separate over any part of the embryo, it leads to compression of that part, perhaps also to the fusion of contiguous structures in that part which ought to have remained separate, and so malformations of that compressed region are produced; when the whole amniotic membrane is ill-developed, multiple and various deformities are the results. It will be seen, therefore, that I have led the reader by a detour through the nosological theory back again to the pressure-theory in teratogenesis, as indeed I indicated I was going to do at the end of the preceding chapter (p. 155). For some years back amniotic pressure has been the most popular theory of teratogenesis among teratologists, and with them it has largely supplanted any notions of disease either of the fœtus itself or of its surrounding membranes. The exact mode of action of the pressure has been supposed to be by causing arrestment of the ontogenetic processes going on in the developing embryo; in this way ontogenetic phases, which are normally transitory and passing, have been rendered permanent, and the results of their permanence are seen in monstrous parts surrounded by normal structures. It has also been stated that the embryo is not subject to diseases at all but only to monstrosities, or that, to change slightly the wording of the conclusion, that the manifestations of the pathology of the embryo are malformations and not diseases, that the "diseases" of the embryo are monstrosities, that embryonic pathology is teratology. Thus, what has been called the embryological theory of teratogenesis has come to replace the nosological or pathological, and in so doing has borrowed from the traumatic theory the notion of long-continued pressure exercised by an ill-developed and unseparated amnion.

Of recent years, however, there have been signs that the nosological theory is not dead. These signs have been manifest chiefly in connection with an offshoot from the nosological theory, with, in fact, the question of the mode of production of the so-called spontaneous or intrauterine amputation of parts. We have thus far traced the main current of the nosological theory without looking particularly at the side currents, the little eddies as it were, which swirl past somewhat in the shade; they, however, are not without importance. In the preceding chapter I have already said something with regard to spontaneous amputations brought about through the agency of the umbilical cord, and it will be remembered that I then pointed out that not funic pressure only but also amniotic pressure had been invoked to explain the solutions in continuity of both the soft and hard tissues in the fœtal limbs. I also showed that there were difficulties in believing that pressure alone could perform the amputations, and that some writers had alleged the existence of morbid processes, of disease in fact, in the skin of the affected parts. The reader will recollect how Menzel (in 1873), in connection with a case of congenital sulci of the digits, found certain changes in the skin of the affected parts which seemed to him to suggest commencing amputation by a downgrowth of epithelium. He thought that in the embryo the normal digitation of the extremities was produced by such downgrowths acting in the long axis of the hand or foot, and imagined that if these came to act transversely or circularly after the original digitation had been carried out, then spontaneous amputations would result. He called the process dactylolysis of an epithelial type. Incidentally he explained syndactyly as due to the absence of the normal separation of the digits by physiological dactylolysis. Longuet, in 1877, also criticised the ordinarily accepted view that amputations are produced by amniotic bands, pointing out that in a case observed by him the sulci were of unequal depth and more evident upon the dorsal than upon the plantar aspect of the foot, and that they were associated with paralytic club-foot; he thought they might all be more satisfactorily explained by the action of an intrauterine disease of the nervous system.

These considerations suggested to some minds the idea that congenital amputations might be an antenatal form of ainhum, that curious disease (at first believed to be peculiar to the negroes of Brazil, but now known to have a much wider racial and geographical range), which is characterised by the appearance of a slowly deepening furrow round the base of a toe (usually the little toe), the swelling of the distal part, the development of a slender pedicle, and the final separation of the pendulous digit. The microscopical changes in ainhum consist in a thickening of the horny layer of the epidermis of the affected toe and of the coats of the larger arteries; in the furrow, some of the epithelial cells are swollen and hyaline, the sudoriparous glands are atrophied, and there is a marked small-cell infiltration. Several articles have appeared on the subject of the relation between ainhum and congenital amputations, including those by G. Beauregard (*Des difformités des doigts*, Paris, 1875), by Brochin (*Gaz. d. hôp.*, xlix. 329, 1876), by Lannelongue (1882), by Reclus (1883–1894), by Jeannel (1886), by Rouget (1889), by Raynaud (1895), and by others. Rouget argued strongly against the identity of the two morbid states; he believed that ainhum affected only the black race, that it attacked only adults and only the toes, and that it had a progressive course ending in separation of the digit; congenital amputations, on the other hand, were met with in all races, affected the fingers as well as the toes, were present at birth, were associated with other malformations, and had a tendency to remain stationary. Reclus pointed out that some of the differences enumerated did not hold good, and was inclined to look to disease of the nervous system of a trophic nature for the cause; and Lancereaux (1894) was of the same opinion. Raynaud came to the conclusion that while it was not proved that ainhum and congenital amputations were the same, yet there were several points in which they strongly resembled each other. It may be added that D. M. Moir (*Indian Med. Gaz.*, xxvi. p. 367, 1891) met with a case of supernumerary little toe in a Mohammedan boy of eight years of age; the deformity affected both feet; and the toes were being separated by ainhum. It does not, however, seem to me that Moir shows reasons for believing that ainhum was really the active process causing separation in this case. It must, I think, be left doubtful whether congenital amputations are the same from the pathological point of view as ainhum; my own opinion is that they are not, and this is supported by the differences in microscopical characters (Broussolle, *Rev. mens. d. mal. d. l'enf.*, viii. 23, 161, 1890). At any rate, it cannot be maintained that the whole discussion on this matter tends in any degree to settle the large question of the relation of fœtal diseases to malformations and monstrosities. It is, as I have said, only an eddy in the main current of the problem.

Another eddy or side current arising out of the large stream of opinion upon the nosological theory is occupied with the regeneration of lost parts. In connection with spontaneous amputations of limbs, J. Y. Simpson suggested that the little nodules seen sometimes on the stump of such defective limbs were attempts at a rudimentary reproduction of the amputated parts. This suggestion is really a begging of the question, for all teratologists are not agreed that a segment of the limb has actually been amputated; but, accepting the preliminary doubt, it may be said that a good deal of evidence has been gathered together to show that in early embryonic life there may be a considerable power of reproduction of destroyed structures, and that in this particular the human embryo resembles the adult form of some of the lower animals. The axolotl, for instance, can reproduce digits which have been removed, and it is a striking fact that the parts reproduced tend to be malformed. Some time ago I asked Professor J. Arthur Thomson, of Aberdeen, some questions on the zoological aspect of this matter. He kindly replied that so far as was known there was—(1) very great power of regenerating lost external parts of considerable size (*e.g.* a limb or lens) in even adult amphibians, such as newts; (2) much less power of doing so in reptiles, but, in lizards, tails and large parts of limbs might be reproduced; and (3) even in birds there have been some striking cases, *e.g.* the notable instance of the regeneration of large pieces of bone or horn in the upper and lower jaws of fighting male storks. I think, therefore, there can be little doubt that similar regenerations of parts are possible during the embryonic phase and perhaps in the early fœtal epoch of human antenatal life. To my mind, and from the theoretical standpoint, it seems more difficult to understand how the parts can be amputated than to admit that they may be reproduced.

To return, for a short time, to the consideration of the main current of the nosological theory of teratogenesis, let me point out some of the recent advances in Embryology and their possible bearing upon this problem. It has come to be recognised, for instance, that the early weeks of antenatal life are occupied with the *formation* of the embryo and its parts, and that the later weeks and months are characterised by the *performance of fœtal functions* and by the *growth* of fœtal parts. Diseases in the strict sense of the word are possible in the later or fœtal period of antenatal life; while in the early or formative period, malformations are the result of interference with the normal progress of affairs. To say that a disease of the fœtus is the cause of its malformation is to invert the order of events; until the part is formed it cannot become the seat of the changes which constitute a disease. As Duval (Bouchard's *Traité de pathologie générale*, p. 161, 1895) puts it, "la malformation, l'état monstrueux d'une partie n'est pas la conséquence d'une maladie subie par cette partie; cet état monstrueux, ce développement anormal constitue la maladie même." This conception of the nature and scope of embryonic as compared with fœtal pathology, of course, alters our views regarding the nosological theory of teratogenesis, whether we look upon that theory as depending upon the diseases of the fœtus itself or upon the maladies of its membranes; in fact it may be said to be fatal to the nosological theory. I have, however, already several times pointed out that there is no hard-and-fast line between embryonic life and fœtal life; all formation is not completed in what we term the embryonic epoch (first six weeks or thereby), neither is the performance of functions limited entirely to the fœtal period (last thirty-two weeks); some of the organs are capable of performing functions and therefore of having diseases in the embryonic period; and there is still some formation going on in the fœtal period, and, therefore, the possibility then exists of some malformations arising. I hold, therefore, that the nosological theory has not been altogether discredited by the new conception of antenatal life which has been arrived at; I maintain that diseases of formed parts of the embryo may occur and possibly interfere with the formation of the other parts, and I think that parts which have been developed monstrously in the embryonic epoch will be very liable to become the seat of disease in the fœtal period. In this way diseases and malformations may coexist in the fœtus and affect each other.

But, it may be asked, how does this conception affect the theory of amniotic disease as a factor in teratogenesis? Two significant facts have of late years been discovered regarding the amnion. It has become evident that the avian method of development of the amnion from the upgrowth of two folds of epiblast and mesoblast round the embryo does not apply to the human embryo: it may be that there is a sinking down of the embryonic disc into the blastoderm and an invagination of the membranes as suggested by Mall (*Journ. of Morphol.*, xii. 395, 1897); it may be that the amniotic sac forms by a vacuolisation of a portion of the inner cell mass as occurs in the bat, and is therefore a closed cavity from the very beginning (M'Murrich, *Development of the Human Body*, p. 131, 1903); or it may be, as Berry Hart has thought, that there is first the formation and then the breaking down of an epiblastic plug to form the cavity of the amnion. If we accept any of these later views on the formation of the amnion it becomes perceptibly easier to understand the formation of amniotic adhesions and bands and pressure; for, if there is a stage of breaking down of tissues in the immediate neighbourhood of the embryo, it is not difficult to imagine an arrest in the breaking-down process resulting in the formation of adhesions. There may, therefore, be no need to invoke the occurrence of inflammation or any other disease of the amnion; defects in the formation of the membrane and cavity will be sufficient to account for the acquirement of adhesions. There is, however, one other fact of recent discovery which requires to be taken into account in coming to a conclusion on this matter. It has been found that the amniotic sac is already formed in the earliest known human blastodermic vesicle; it is present in Peters' specimen of a few days old. The formation of the amnion, therefore, precedes the formation of the embryo. The conclusion I draw from this fact is that the amnion is fully formed and capable of performing functions before the embryo has passed through the formative or strictly embryonic stage. I think, therefore, that, after all, it may be scientifically accurate to speak of disease of the amnion as a possible cause of deformities of the embryo; amniotitis or amnionitis may be a pathological possibility and a cause of teratological developments in the embryo. At the same time, it appears to me that defective development of the amnion and possibly the pressure which it thus brings to bear upon the plastic embryo are much more likely methods for the production of teratological conditions. Thus we have extracted from the pressure theory and the nosological theory of teratogenesis the really essential and valuable elements; we hand these on to the embryological theory to explain some conditions in it otherwise difficult of comprehension (*vide* Chapter XII.).

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CHAPTER XII

The Embryological Theory in Teratogenesis: Historical Sketch of the Theory; Embryology an Explanation of Teratology; Arrested Development; the Amniotic Factor in Teratogenesis; Experimental Teratogeny in the hands of Geoffroy Saint-Hilaire, Allen Thomson, Panum, Schrohe, Lombardini, Dareste, Féré, and others; the Germinal Factor: Summary.

The latest of the teratogenetic theories, which has been called the *embryological*, now demands consideration. It is the latest; it may also be the last, for I believe that if all the facts were known they would be found to fit this theory; but it is dangerous to speak of finality in these matters, and it savours of presumption, for finalism, with its suggestion of infallibility, is obnoxious to the scientific mind. The way is not yet closed against the advance of new theories; but they will require to be very satisfactory, very conspicuously sufficient to explain the phenomena, and very convincingly efficient to overcome all the difficulties, if they are to displace the embryological theory in teratogenesis.

If the reader will at this stage re-read Chapter VII. (pp. 72 to 80), he will gain a general idea of what is meant by the embryological theory of the formation of monstrosities and malformations. He will find there an Ariadne-thread to lead him through the labyrinthine mazes of Teratology, a threefold thread, with the three factors of embryonic physiology, the action of the amnion, and germinal pathology forming its constituent strands. He will be led to focus his gaze upon Embryology; to scrutinise all the phenomena of embryogenesis and of ontogenesis, so far as they are known; to look for his clue in the normal processes of formation and evolution of the organism. He will discover that the most complex and perplexingly intricate monstrosities and malformations become perceptibly less complex and less intricate when viewed in the light which comes from the study of the development of the parts affected. The origin of a landscape, with its diversity of features,—mountain, valley, river, gorge, lake, and crag,—may seem inexplicable; but the eye of the geologist pierces below the surface, and, conjuring up the visual image of the prehistoric mutations of the component parts of the earth's crust, reveals the processes and explains the methods by which all these things came to be just what they are. So must the teratologist look at a fully-formed malformation, not with his gaze riveted upon what it now is, but in imagination dwelling upon what that malformed part was in the second, in the third, or in the fourth week of the intrauterine life of the embryo; he will then begin to see, like the geologist, below the surface, and to learn from present things what past conditions were. Let us now study more in detail this embryological theory; let us see how Embryology helps us to understand Teratology.

The embryological theory in teratogenesis dates from the time of Harvey, who laid the foundation-stone of it in his treatise on *Generation*, a work which, it is interesting to remember, he was little inclined to publish, and only "ventured it out of his hands with reluctance" after receiving the solicitations of Ent. To Ent, indeed, we owe it that the *Exercises on the Generation of Animals* (with the famous passage on malformations) saw the light in 1651. There, in the sixty-ninth exercise (I quote from Willis' translation of the *Works of William Harvey*, Sydenham Society, p. 487, 1847), are the following sentences: "In the fœtuses of all animals, indeed that of man inclusive, the oral aperture without lips or cheeks is seen stretching from ear to ear; and this is the reason, unless I much mistake, why so many are born with the upper lip divided as it is in the hare and camel, whence the common name of *hare-lip* for the deformity. In the development of the human fœtus, the upper lip only coalesces in the middle line at a very late period." In this passage, Harvey, without the help of the microscope it must be remembered, laid down the great principle of malformation by arrest of development; and, although he was ignorant of the exact organogenetic processes by which the parts about the mouth were actually developed, yet he saw the possible results of their retardation, and so, as has been said, laid the foundation-stone of the embryological theory of monstrosities. It must be confessed, however, that neither Harvey himself, nor those who immediately succeeded him in his own country or abroad, built much upon the foundation-stone thus laid. Not till a century had passed did any sign of building actually appear, and then little more than indications of the walls of the future edifice were to be seen above ground. In A. von Haller's writings (*Operum Anatomici Argumenti Minorum*, iii. p. 135, 1768) there is the indication of the idea that ectopia cordis may be due to the persistence of the stage in development (seen in the chick) when the heart lies uncovered by muscles and ribs; some years later (1772), C. F. Wolff (*N. Comment. Acad. Scient. Imper. Petropolitanæ*, xvii. 540, 560, 1773) explained the origin of both ectopia cordis and exomphalos by absence of the normal closure of the abdomino-thoracic walls; and J. H. T. von Autenrieth (*Observationum ad historiam embryonis facientium*, p. 38, 1797), towards the close of the eighteenth century, extended the idea of arrested development till it included not only all the monstrosities by defect of formation, but also the double terata.

It was in the nineteenth century, however, that this theory began, like a tree, to spread out its branches in all directions, and in ways and with results undreamed of by the writers who helped to plant it. J. F. Meckel (*Handbuch der path. Anatomie*, pp. 48, 51, etc., Leipzig, 1812), for instance, discussed in detail the various arrested developments (*Hemmungsbildungen*), and pointed out that some of those which occurred in the human subject represented conditions which were to be found in the lower animals. So, out of these observations, grew the belief that the human embryo in his antenatal existence is first a worm, then a fish, then an amphibian, and then a bird; that, in other words, he climbs up his genealogical tree, which, as it happens, is also the zoological scale. Of this view I have elsewhere spoken (Chapter II.); it is not now accepted unreservedly, but it had a wide vogue during the nineteenth century. The idea that malformations were arrested developments was not, however, inseparably bound up with the notion of the ascent of the embryo through stages corresponding to zoological sub-kingdoms; its applicability to teratological problems was independent thereof, although it must be admitted that the idea of the existence of a parallelism between phylogeny and ontogeny was helpful in explaining malformations which did not resemble any stage in the development of the human embyro. Hare-lip, cleft palate, spina bifida, the uteris bicornis, exomphalos, and ectopia cordis were so easily and evidently explicable as arrested developments that they ensured for the theory a permanent place in teratogenesis; but there were other anomalies which found no such easy explanation, and in their case recourse was had to the facts of zoology.

Shortly after Meckel (*op. cit.*) wrote his work on Pathology, and about the time when F. L. Fleischmann (*Bildungshemmungen der Menschen und Thiere*, p. 24 *et seq.*, Nürnberg, 1833) was expanding his suggestions and theories, a great discussion arose regarding the laws of development, and in the course of this controversy teratological cases and problems were freely referred to. It would lead us too far into general biology to follow out all the ramifications of the theories and statements made by E. Saint-Hilaire (1822), by Serres (1824, 1832, and 1860), by I. Saint-Hilaire (1836), by Bischoff (1842), by Darwin (1868, etc.), and by a legion of other scientists, investigators, and philosophers; but certain points deserve at least a passing reference.

There was, for instance, the question of the influence of one set of organs of the body over the others, especially in relation to the cases in which one system was the seat of malformation. Some writers maintained that the nervous system, and especially the spinal cord, was the centre for the regulation of the formation of all the parts. Certain teratological facts seemed to support this view, such as the absence of the olfactory nerves in cyclopia (in which there is often no nose to be found), and unilateral atrophy of the spinal cord in cases of congenital absence of one limb; other facts, however, seemed to tell against it, such as the advanced development of the fœtal tissues in anencephaly, the presence of many organs and parts in the placental parasites (allantoido-angiopagous twins) which have no brain and no spinal cord, the absence of any alteration in the spinal cord in cases of absence of one limb (as in the three-legged kitten described by me in the *Interstate Med. Journ.*, vii. 367, 1900), the ability of some of the lower forms of life to develop without a nervous system, the comparatively late date in antenatal life when the nervous tissues reach functional maturity, and the absence in some monstrosities of the nerves (*e.g.* vagi) supplying certain viscera along with the presence of the viscera themselves. It would seem, if we take a fair and comprehensive view of the facts, that the nervous system has not the powerful regulating action upon development and growth that was once attributed to it; but it would also seem that the absence of the nerves supplying any part of the body is not altogether without results upon the structure and functions of that part. It may also be admitted that it is quite possible that this influence may be either greater or less during early antenatal life than it is after birth.

The failure, for want of evidence, of the theory of the supremacy of the nervous system over the other systems was, doubtless, partly the cause why some writers (*e.g.* Tiedemann and Serres) adopted the view (as old as the time of Aristotle, and possibly older) that the heart and vessels were the controlling factors in the formation of the rest of the organism. According to this view, anencephalus, hypospadias, hare-lip, absence of limbs, and exstrophy of the bladder were to be explained by incomplete development of the vessels supplying the parts which were malformed. The idea was supported by such facts as the small size of the vertebral and internal carotid arteries in anencephaly alongside of the large size of the external carotids, by the small dimensions of the external carotids and the cephalic arteries in microcephaly, and by the occurrence of malformations in the embryo when the vascular area showed defects in its formation. These facts, however, may be perfectly true, and yet it does not follow that the vascular defect was the cause of the malformation; it may, indeed, have been the consequence of it.

Another question which greatly exercised the minds of teratologists and embryologists in the first half of the nineteenth century was in relation to the direction of developmental processes: some (*e.g.* Serres) believed that formation took place from the periphery towards the centre (centripetal development), and that, therefore, the vessels and nerves preceded the heart and cerebro-spinal axis; while others (*e.g.* Baer) maintained the theory of centrifugal development. Apparent exceptions to both theories can easily be found in Teratology, and it was necessary for Embryology to make marked advances before these questions and their corollaries could be satisfactorily dealt with. In the meantime these difficulties produced the effect of making the teratologists look further back in antenatal history for the causes of monstrosities; so their attention came to be concentrated upon the embryonic epoch, before the blood vessels and nerves have begun to be functionally active.

Let us now consider to what extent a knowledge of embryonic physiology or embryology (in its limited sense) can explain monstrosities and malformations; let us take the first strand of the Ariadne-thread that is to lead us securely through the mazes of Teratogenesis.

We may, very suitably, begin with Harvey's hint given in connection with hare-lip, in other words with the idea of arrested development. There are many stages in ontogenesis, as the perusal of Chapters III., IV., V., and VI. has informed the reader, and it may be taken as possible that arrest may occur at any one of them and in any part of the embryonic organism. There is, for example, a stage when the limbs are but buds from the trunk; should their formation be then arrested an explanation is forthcoming of some of the forms of ectromely. There is also a stage when the heart is external in position; it may remain so, giving rise to ectopia cordis. There is, again, a stage in the internal formation of the heart when the ventricles communicate with each other; this state may persist and the fœtus be born with that organ possessing a single ventricular cavity. Normally, the second branchial arch by its continued growth covers over and then shuts in the sinus præcervicalis; an arrest in its growth will leave a communication between this sinus and the exterior. There is at one time in embryonic life the peculiar arrangement of vessels known as the aortic arches; by a series of complicated changes some of them disappear and others remain or are fused together to form new vessels; arrests of different parts and at different times will cause vascular anomalies which are easily enough understood when the ontogeny of the parts is clearly comprehended.

The reader will have noted that I have already referred to two different ways in which arrested development may show itself: it may be evident in stoppage of the formatiom of a part, or it may be observed in the persistence of a part which ought to disappear. There are, however, yet other ways in which it may act: two parts which ought to unite may, by defect of growth, fail to do so, and so give rise to such anomalies as hare-lip and cleft palate. The cause may possibly be a sort of unpunctuality of one part, which does not come forward in time to meet another, and then is prevented from ever doing so by the progression of other and intermediate parts. It is possible, also, that in some malformations there may have been an absolute non-formation of a part or organ, with a consequent coming together of structures which are normally far apart; this is an explanation which may serve to account for the cyclops fœtus. Again, parts which ought to have grown out of one situation into another may be late in doing so or may fail altogether to do so. By this mechanism it is probable that we must account for the hernia of the intestine into the root of the umbilical cord, sometimes found in the new-born infant. At an early stage the intestinal loop has, so to say, the right to lie in the umbilical aperture; but it ought long before birth to have been withdrawn into the peritoneal cavity; it is not so retracted, and thus the hernia or its subsequent development, a fæcal umbilical fistula, is produced. Yet again, some structures which are pervious during early embryonic life close at a later stage; arrest may, however, seize upon them, and their patency remains, as is seen in an umbilical urinary fistula (due to persistence of the urachus) or in a patent ductus arteriosus. Parts which ought to atrophy or at least become rudimentary in fœtal life, such as the Müllerian ducts (and their derivatives) in the male, may suffer an arrest in their process of disappearance and remain as malformations by excess. An example of this is found in spurious hermaphroditism of the male, in which in addition to testicles, prostate, and the associated ducts, there are found Fallopian tubes and a uterus.

Without multiplying instances, it becomes clear, therefore, that simple arrest of development or of growth in the embryo serves to account for many monstrosities and malformations. For some anomalies, however, this explanation fails, and other modes of origin must be adduced.

It would seem that in some instances there is a process of true excessive development. For example, the presence in the new-born infant of a distinct tail, due to supernumerary coccygeal vertebræ, would seem to require an explanation of this kind; but all so-called "tails" are not truly of this nature. Some cases of external hermaphroditism (spurious) may also be included in this group; thus, the clitoris may be abnormally large and so cause a superficial resemblance to a penis. In a very curious group of malformations, the heterotaxies (*i.e.* those in which the organs of the body are inverted, are arranged as if seen in a mirror), it would appear as if arrest and excess of development were combined in their teratogenesis; thus instead of an aortic arch on the right side, disappearing while the corresponding one on the left side remains, the left one may disappear and the right one remain. So-called transposition of the great vessels is not therefore really a transposition but a combination of arrest and persistence.

The embedding in the body-cavities of parts or derivatives of parts which are normally external would seem at first sight to be inexplicable by arrest of development. On further consideration, however, some of the difficulty disappears. Is not the whole nervous system (securely closed in within the spinal column and cranial cavity) originally external? Is it not ectodermic in its origin? Is there not, further, a stage in ontogenesis when the thoraco-abdominal cavity is open and in a sense external? It is not, upon reflection, so difficult to imagine a piece of the ectoderm becoming included in one or other of the cavities, as the cerebro-spinal nervous tube is included within the cranio-spinal canal, if these cavities are perchance delayed in closing. In the same way, if a branchial cleft is too long in being shut off from the exterior, a neighbouring structure may be caught, as it were, or snared in it. When a simple tube, such as that which gives origin to the brain, undergoes a series of complicated flexures and bendings, it is quite conceivable that if these bendings are late in being achieved neighbouring structures may be inserted between them. It is perhaps in this way, and by a process which we may describe (to borrow a French word) as "enclavement," that some intracranial dermoid cysts may be produced.

If, as has been supposed, certain openings and canals, such as the anus and the vagina, get their lumen by the breaking down of ectodermic plugs, then it is easy to understand how an arrested breaking down would lead to imperforation or to septa or narrowings of these parts.

It is evident, therefore, that the principle of arrested development is fertile in yielding explanations of many of the varieties of monstrosity and malformation; but there are cases which it is inadequate to elucidate. For instance, there is sympodia, that curious teratological state in which the lower limbs are not only fused together into one but have evidently been rotated during the fusing; there are the cases of complete and partial congenital amputation and of other forms of mutilation; and there are all the types of true excessive development and double monsters, symmetrical or asymmetrical. Further, although arrested ontogenesis may interpret many anomalies, it, after all, does not give any hint as to the *causa causans*; we have, as yet, left unanswered the question, Why is there an arrest at all? To explain some of these difficulties we must pick up the second strand of the threefold Ariadne-thread that is to guide us through the bewildering passages of our teratological labyrinth.

A consideration of the amniotic membrane throws some light both upon these monstrosities that are not explicable by simple embryonic arrest, and also upon the *causa causans* of the malformations which are so explicable. I have already, in writing of the nosological theory of teratogenesis, opened up the possible modes of action of the amnion, and I need not here repeat much of what appears in the preceding chapter. It must, for the present, be left uncertain whether the amnion acts upon the embryo by pressure due to non-separation of the membrane from the surface of the organism by defect of the liquor amnii, or by disease of the membrane of an inflammatory kind leading to the production of adhesions which compress the embryonic parts and organs; it must also be conceded that the exact mode of formation of the amnion in the human subject is unknown. At the same time, it is well known that the amnion may be found adherent to the fœtus at birth, and that the fœtus, which is thus brought into connection with it, is generally malformed in the affected parts; it is also clear from embryological studies that there is a time in early embryonic life when the amnion lies in close contact with the embryo; and, finally, it has been shown by the early gestation-sacs of Peters and others that the amnion is present before the embryo. In addition, we know, from the experiments in teratogeny of Dareste and others, that defective development of the amnion in the chick is constantly associated with malformations; but I lay no great stress upon this fact, for the formation of the avian amnion is evidently different from that of the mammalian one. I think, therefore, that these facts lead us to the conclusions: (1) that the action of the amnion may be teratogenic in the human subject; (2) that certain multiple deformities, such as sulci and amputations of the limbs and digits, and adhesion of the fœtal membranes to the cranium or abdomen or face, must be regarded as specially amniotic in origin; (3) that non-separation of the amnion from parts of the embryo in the stage of architectonic activity (*e.g.* in the case of the face during the growth and approximation of the various processes to each other) may be the actual means of arresting these developmental activities; and (4) that in some monstrosities not explicable by simple arrest (*e.g.* in sympodia and cyclopia), the amnion may by exercising pressure upon contiguous parts lead to their partial or complete fusion.

The reader may now say, and there is perfect justification for the objection, that after all, while the amniotic factor serves to explain some monstrosities which arrest of development does not account for, and in some measure elucidates the cause of the arrested ontogenesis itself, still this does not bring us to the ultimate cause of these monstrosities and malformations. In a word, we are left face to face with the problem of the cause of the amniotic defect, disease, or adhesion. What is it that prevents the development of the amnion in its normal way and leads to its arrest? The arrested development of the embryo is, let us admit, due to an arrested development of the amnion or to disease of it; but what arrests the amnion or sets up disease in it? An attempt has been made to answer this question along the lines of experiment; it has not until recent years enjoyed any measure of success, but it has thrown some light, albeit not of a piercing kind, upon the matter. Let us then, as briefly as may be, consider the subject of Experimental Teratogenesis.

Experimental Teratogeny.

Most of the experiments with regard to the causes of monstrosities have been made upon the chick during incubation, natural or artificial. The reasons for this are obvious. The artificial hatching of eggs was carried out long ago in Egypt, and the knowledge of the methods employed and the practice of the art spread to Europe towards the close of the sixteenth century. It was in the partial failure of the attempts then made that the germ of the science of experimental teratogeny lay. It was often found that many of the chickens thus artificially incubated were deformed. Such was the experience of Olivier de Serres (*Théâtre d'agriculture*, v. c. ii.) in 1600; and in the records of the Royal Society of London for January 16, 1679 (T. Birch, *History of the Royal Society of London*, vol. iii. p. 455, 1757), the following passage occurs: "Mr. Henshaw further gave an account of the manner, how Dr. Kuffler hatched chickens by the help of furnaces, the process of which he had seen; which was that the doctor had a wire-grate placed over a balneum at a foot distance with a cover over, pulled up by a pulley; in which grate he set the eggs, and so turned them every day for eighteen days together: then he laid them on a hair-cloth in a stove near the ash-hole, where they hatched themselves with their own bills; in which stove he kept them for three days, till they could feed themselves, which was when the yolk was consumed in their bellies. He added that in Egypt they do this with camel's dung. Sir Jonas Moore remarked that Sir Christopher Heydon together with Drebell long since in the Minories hatched several hundred eggs; but mentioned not the way; but that it had this effect, that most of the chickens produced that way were lame and defective in some part or other." Such was the statement made by Sir Jonas Moore regarding the process of egg-hatching as carried out in England before 1679; but he added to his statement the following somewhat startling remark that "Drebell had an art, by which he could produce a fly in an hour's time anywhere." We are not told whether Drebell's flies like his chicks were usually malformed. Dareste, in his work (*op. cit.*, p. 32), quotes from Paris's "Memoir on the Physiology of the Egg read before the Linnean Society of London, the 21 March 1809," the following sentence: "During the period that I was at College, the late Sir Busick Harwood, the ingenious Professor of Anatomy in the University of Cambridge, frequently attempted to develop the egg, by the heat of his hotbed; but he only raised monsters, a result which he attributed to the unsteady application of heat." I have looked up the article by J. A. Paris referred to above (in the *Trans. Linnean Soc. Lond.*, x. 304, 1811), but have failed to find the sentence quoted by Dareste; but I happened upon the following interesting statement, which has a bearing upon the question of antenatal pathology: it is recorded that a hen had its leg broken, and that three days subsequently it laid several eggs destitute of shells, and Paris thought that the calcareous matter designed for the shell had been employed in the regeneration of the bone.

From these quotations (and from others which could be given) it is clear that the artificial incubation of hens' eggs was practised and the frequent teratological results known before the beginning of the nineteenth century. To Etienne Geoffroy Saint-Hilaire, however, the honour apparently belongs of having conceived and carried out the idea of turning these experiments to account in the investigation of monstrosities and malformations. In the work of the younger Saint-Hilaire (*Histoire des anomalies,* iii. 500, 1836) there are references to the experiments made by his father and to the journals and books in which the results of these experiments had been related. At first (in 1820 and 1822) he, Etienne Geoffroy Saint-Hilaire, employed natural incubation; but, on account of the small number of observations possible by this method, he adopted artificial incubation in 1826 (*Journ. comp. du dict de sc. méd.,* xxiv. 256, 1826). His object was to produce anomalies in the chick at will by disturbing development in different ways during the early days of incubation. Apparently the time when most of the experiments were commenced was after the third day of incubation. Various plans were used, such as shaking the eggs, pricking them at various points, keeping them in a vertical position, and partially covering them with wax or varnish; and the result was the production of a relatively considerable number of anomalies, both simple and complex, such as triocephaly, atrophy of the eyes, eventration, and spina bifida. No double monsters were got. Isidore Geoffroy Saint-Hilaire states (*op. cit.*, p. 503) that he repeated the experiments of his father and made in addition others in which he tried to produce monstrosities by disturbing incubation at an earlier date than the third day; the result was that he obtained no monstrosities but got either no chicks at all or only dwarf ones. He, therefore, came to the conclusion that monstrosities were principally caused by disturbing conditions acting when certain of the organs of the embryo were developing. These experiments were carried out in 1831. Dareste, from a consideration of all the available information, believes that Saint-Hilaire proved, in opposition to the views of Wolff and Meckel, that a change in the physical conditions which determine development may modify the development itself, and that, in consequence, anomalies and monstrosities do not arise only from a virtuality placed in the germ before or at the time of fecundation.

Other observers seem soon to have repeated these experiments of the Saint-Hilaires with or without alterations. Thus, Allen Thomson, Professor of the Institutes of Medicine in the University of Edinburgh, writing in 1844 (*Lond. and Edinb. Month. Journ. Med. Sc.*, iv. 486, 1844), made the following statement: "In 1833 and 1834, I made several series of experiments of the same kind with these now mentioned" (he is referring to the work of E. Geoffroy Saint-Hilaire), "and with a similar result." Further, Thomson says that in the course of a long series of experiments on incubation, carried on at various intervals, he had been so fortunate as to meet with two instances of very early double malformation in the bird. It does not appear from the context whether the incubation-conditions had been altered in any way in these two cases; but in another part of the same article (*loc. cit.*, p. 579) he wrote, "Again, I may remark, I have subjected at different periods nearly a dozen double-yolked eggs to incubation, and have never succeeded in obtaining a double monster, nor even two embryos at the full period from any of them." Thomson is most tantalisingly silent as to all the details of his experiments, but his silence may be in part accounted for by the low value he seems to have set upon them as means of elucidating the problems of Teratology. While allowing that malformations might be to some extent under the influence of mechanical causes, he thought that there must be some original cause of an unknown nature existing in the ovum or germ to account for the constancy with which certain forms return, for their symmetry, and hereditary character.

During the fifty years that followed the experiments of the Saint-Hilaires and Allen Thomson one observer stood out supreme in the field of artificial teratogeny. I refer to Camille Dareste, who, between the year 1855, when he published a paper on the effect which varnishing the shell has on the development of the chick, and 1891, when the second edition of his large work (*Recherches sur la production artificielle des monstruosités*) appeared, carried out an enormous amount of experimental work, and embodied the results in a long series of monographs and articles. If Dareste was not the first to conceive the idea of the artificial production of monstrosities as a means of elucidating their causation, he was, beyond all question, the one to whom the existence of experimental teratogenesis as a definite department of Biology is due. Others, such as Panum, Schrohe, Engel, Lombardini, Lereboullet, Knoch, Szymkiewicz, Maggiorani, Gerlach and Koch, and Warynski and Fol, were at work contemporaneously with Dareste, and many of them added largely to our knowledge of the subject; but none of them can be said to have left his impress upon it in the way that Dareste did, or to have carried out his experiments with such whole-souled devotion. Before referring to Dareste's work, I may briefly note the nature of the experiments of the other authors named above.

F. P. Liharzik (*Das Gesetz des menschlichen Wachsthumes*, Wien, 1858) found that if he placed the eggs vertically in the stove after the mid-term of incubation, he got chicks with the part which had been lowest better developed than the rest; but he got no monstrosities. P. L. Panum in his *Untersuchungen über die Entstehung der Missbildungen zunächst in den Eiern von Vögel* (Berlin, 1860), and later in two journal articles (*Nord. Med. Ark.*, i. 1, 1869; *Arch. f. path. Anat.*, lxxii. 69, 165, 289, 1878) wrote at considerable length upon malformations in chicks and fish. He advanced a cellular theory to explain both the normal and teratological forms assumed by the fœtus, and suggested as the cause of the cellular perturbations in monstrosities a sort of inflammation of the embryonic structures; according as the cause acted before or after the formation of vessels, the inflammation was parenchymatous or vascular. In this respect, therefore, Panum, it is to be noted, had recourse to a nosological explanation of the disturbances in embryogenesis. It is not clear that there is any justification for this view; but at the time when Panum wrote, the suggestion was a perfectly fair deduction, for much that we now know regarding the early stages of development was then unknown. In his experiments upon eggs he chiefly employed changes of temperature as the teratogenic agent, and he found that a rise in temperature was more dangerous to the embryo than a fall and could not be borne so long, and that a slow lowering of temperature had greater results than a rapid fall. He found that the younger embryos were, the more likely were they to become monstrous and to show extensive anomalies; it was rare that disturbing causes produced malformations when they came into play after the seventh or eighth day of incubation. Panum gave a very interesting account of certain general conditions of the embryo, and named the embryos so affected flattened, cylindrical, nodular, and atrophic; he also described in detail some malformations of the vascular area of a very interesting kind. His work was most valuable, but on its experimental side it did not approach that of Dareste either in extent or in accuracy. Joseph Engel (*Wien. med. Wchnschr.*, xv. 17, 33, 49, 1865) made experiments somewhat resembling those of Panum. It should be stated that Adam Schrohe (*Untersuchungen über den Einfluss mechanischer Verletzungen auf die Entwickelung des Embryo im Hühnerei*, Giessen, 1862) attempted to produce monstrous chicks artificially by a new method, namely, the wounding of the embryonic area or embryo with a cataract knife; he met with a measure of success, but the method was faulty, and the same criticism applies to the experiments of Lombardini (*Forme organiche irregolari negli uccelli e nei batraci*, Pisa, 1868). Lombardini employed electricity as his traumatic and teratogenic agency, and experimented both upon chicks and upon the ova of frogs; he obtained 19 deformed embryos (ectopia cordis, general dropsy, amniotic adhesions to the head, etc.) out of 95 eggs, 33 dead embryos, and 43 that had undergone no change; and the time when he passed the electric current through the eggs was between the second and ninth day of incubation.

Lereboullet (*Ann. des sc. nat. zool.*, s. iv., xx. 178; s. v., i. 113, 257, 320, 1863 and 1864) also had carried on experiments on fish ova (the pike was the fish chosen); but had, on the whole, got negative results. The methods he employed were temperature variations, shaking the ova during fecundation, and the like; and he believed that his experiments showed that only arrested developments, deformities, and atrophies were due, and that only occasionally, to external agencies. He thought that the cause of monstrosities might be inherent to the constitution of the egg itself, and thus in no way dependent upon external states. Dareste refers to the work of Knoch, of Moscow, published in 1873; the experiments were performed upon salmon embryos, but they were (in Dareste's opinion) too incomplete to be of value in the drawing of conclusions. In 1875, Szymkiewicz (*Beitrag zur Lehre von den künstlichen Missbildungen am Hühnereie*, Wien, 1875) attempted, by wounding the embryo chick, to produce deformities; but the embryos either died or showed too complex deformities to be of value in teratogenesis. S. Warynski and H. Fol (*Rev. méd. de la Suisse Rom.*, iii. 395, 1883; *Compt. rend. Acad. d. sc.*, xcvi. 1674, 1883) also tried traumatic measures for the production of monstrous chicks. They cut a small window in the egg-shell, wounded the embryo with a Paquelin thermocautery or a scalpel, replaced the fragment of shell, fixed it in position, and returned the egg to the incubator. They obtained monstrosities such as heterotaxy, duplicity of the heart, and spinal cyphosis. Further details of the chicks with double hearts were given by Warynski in 1886 (*Sur la production artificielle des monstres à cœur double chez les poulets*, Thèse, Geneva, 1886). In 1883, L. Gerlach and H. Koch (*Biol. Centrlbl.*, ii. 681) succeeded in getting dwarf embryos by partially varnishing the eggs; more correctly, they got embryos one part of which was smaller than the others. In two cases they found the monstrosity known as omphalocephaly. C. Maggiorani (*Influenza del magnetismo sulla embriogenesi*, Roma, 1885) tried the effect of incubating eggs laid between bar magnets, and found that arrested developments were four times more numerous among them than among eggs hatched in the usual way. Magnetism was also the means employed by Windle some ten years later, as we shall see. A. Marcacci (*Ann. di Univ. libera di Perugia*, i. 171, 1885–86; *Bull. d. sc. med. di Bologna*, 6 s., xxii. 5, 1888; *Arch. ital. de biol.*, ix. 58, 1887) experimented upon eggs by shaking them either in a vertical or in a horizontal plane by means of a somewhat ingenious apparatus; the results seem to have been rupture of the vitelline membrane and death of the embryo chicks, but sometimes anomalies in the rate of growth were obtained. Tarulli (*Atti e rendic. d. Accad. med.-chir. di Perugia*, ii. 121, 1890) returned to one of the older methods of disturbing incubation; he employed coating the eggs with oil; and he regarded the death of the chick as due not only to the interference with respiration, but also to the altered pressure within the shell, and to the change in temperature due to the difference in evaporation.

While these different writers and experimentalists were engaged in their researches, Camille Dareste was steadily working at artificial teratogeny in Paris, and publishing from time to time the results of his researches. It is time that I gave a summary of his labours in this field of study, which he made so peculiarly his own. Although his death did not take place till 1899, yet his life-work was accomplished between the years 1855 and 1891; he published, it is true, two articles, one on the action of mercurial vapours on the embryo (*Compt. rend. Soc. de biol.*, Paris, 9 s., v. 683, 1893) and the other on the effect of electricity (*Compt. rend. Acad. d. sc.*, Paris, cxxi. 955, 1895), after the year 1891, but the appearance of the second edition of his large book in that year may still be looked upon as the close of the most active part of his scientific life. It was not long before Dareste found that the various agents which he used to produce disturbances in embryogenesis all led to the appearance of the same monstrous forms; there was no relation between the nature of the teratogenic cause and the kind of teratological result. Consequently he did not much employ varnishing the eggs, fixing them in one position, and the like, but used, almost solely, variations of temperature. Having found the normal range of temperature for normal incubation, he raised or lowered the heat and got teratological results. In one set of cases only was he able to predict the character of the monstrosity to be produced: when he unequally heated the shell he obtained elliptical deformities of the blastoderm and vascular area. From his numerous experiments made by varying the temperature during incubation, and from the careful examination of the monstrous chicks thus produced, Dareste was able to draw a great many conclusions, most of which have already been indicated in the sketch that I have given of the embryological theory of teratogenesis. He drew, for instance, the deduction that teratogeny was always the consequence of a modification of embryonic development, and instead of basing it upon theory he showed facts. He decided, therefore, against the nosological theory. He indeed admitted the existence of diseases in the embryo (such as dropsy, of which he gave a very complete account); but he looked upon them as producing death or disorganisation, not malformation, of the embryo. He laid great stress upon arrest of development as the method by which single monsters were produced; and, with the single exception of heterotaxy, he regarded all malformations of the single embryo as explicable by arrest. He noted that the earlier the anomalies were produced in embryonic life the more grave were the resulting teratological states. He differentiated between *hemiterata* in which the arrest of development was quite local and was due to a teratogenic cause of little intensity, and the *monstrosities* proper in which it affected a whole region and was the result of a strong teratogenic influence. He described the development of blastoderms without embryos; defect of differentiation of the embryonic area into the embryo and the vascular area; the arrests of development of the blood islands and the resulting vessels of the vascular area; the arrests of development of the allantois; and, what is of the greatest interest to us in connection with the present subject, the arrested development of the amnion, which is the primary fact of most embryonic monstrosities ("fait initial de la plupart des monstruosités embryonnaires"). He demonstrated that triocephaly and cyclopia are due to arrest of development of the anterior cerebral vesicle, the result of premature closure of the anterior part of the cerebro-spinal groove; he discovered and explained the curious monstrosity called by him omphalocephaly; he showed that anencephaly, pseudencephaly, and exencephaly all result from the total or partial compression of the cerebral vesicles; and he described how sympodia arose from arrest of the caudal fold of the amnion, how exomphalos was due to defective or arrested formation of the thoraco-abdominal walls, and how ectromely was caused by an arrest in the formation or development of the limbs. He never succeeded in producing double monsters artificially by altering the incubation conditions; but he, nevertheless, threw a great deal of light upon their origin. He believed them to be produced in most cases, if not in all, by the union and fusion of two embryos formed on the same cicatricula or germinal vesicle, and he, therefore, thought that the existence of twins was determined prior to the commencement of incubation, and probably as the result of polyspermy or the entrance of more than one spermatozoon into the ovum. He explained, in a reasonable way, the origin of the curious acardiac, acephalic, and anidean placental parasites; and he showed that, in the absence of a twin embryo, such very rudimentary forms ("with an absence of solidarity") might be initiated but failed to get beyond the earliest stages of development; if a second embryo with a heart were present, they might be supported and kept in life by it, and so be carried on to a later phase of organogenesis.

One might easily refer to many other interesting questions in teratogenesis opened up or cleared up by Dareste, but those alluded to seemed to the writer to have special importance. A conclusion of great value that followed upon the whole research was the similarity of the monstrosities met with in the chick and those found in the mammalia and especially in the human subject. In this fact Dareste found the germ of the hope that the causes active in the chick in teratogenesis might yet be found to apply also to the human subject, and that thus human teratology might likewise be elucidated.

An obvious defect or want in all Dareste's work, however, was found in the nature of the teratogenic agents employed. One could not imagine human or mammalian monstrosities arising on account of variations in the temperature of the surrounding parts (save in the rarest circumstances); and electricity, shaking, deficient supply of oxygen and the like seemed out of the question. This remark applied equally to the work of the other experimenters of Dareste's time; even the traumatic means adopted by Warynski and Fol and others could hardly be imagined as having their representatives in human teratogenesis. Experimental teratogenesis, therefore, although it had cleared up much that was dark in the mode of production of monsters (*e.g.* the compressing power of the ill-developed amnion), had left in all its native obscurity the great problem of the *causa causans.* C. Giacomini (*Giorn. d. r. Accad. med. di Torino,* Nos. 6 and 7, 1889), indeed, had tried experimentally to produce monstrosities in mammals; he had used pregnant rabbits and had drawn off some of the fluid from the blastodermic vesicle, introduced a foreign body into it, and exercised pressure upon it; he had succeeded in arresting development to some extent, and had in some cases met with an atrophic embryo; but the general results were not hopeful for the revelation of the deep-seated causes of monstrosities. L. Blanc's experiments on the effect of bright light upon the chick embryo during incubation (*Compt. rend. Soc. de biol.,* 9 s., iv. 774, 969, 1892; v. 938, 1893) did not seem to help the teratologist much in his search for the explanation of the cause of the arrested development of the amnion; while B. C. A. Windle's observations (*Journ. Anat. and Physiol.,* xxix. 346, 1894–95) on the influence of electricity and magnetism on chicks and trout ova left in the mind of the observer himself the idea that the former agency (electricity) produced an arresting effect upon development, but that the latter (magnetism) could not be definitely said to produce any effect at all. Experimental Teratogeny, therefore, had not, up to 1894, thrown light upon the cause of amniotic arrests of development, although it had established amniotic defects as the most probable cause of the monstrosities themselves.

About this date (1894) Charles Féré began his series of observations. He took the hen's egg as the subject of experimentation just as earlier experimentalists had done; but by the use of chemical substances, microbic toxines, and venin as his teratogenic agents, he brought the whole subject into line with general pathology and made the facts applicable to the problems of Human Teratology. Féré's experiments and their results were published as a long series of articles chiefly in the Proceedings of the Society of Biology of Paris (*Compt. rend. Soc. de biol.,* Paris) between 1893 and the present year (1903); but papers also appeared in the *Journal de l'anatomie et de la physiologie* and in the *Archives d'anatomie microscopique.* He summarised most of the results in an article contributed to the Jubilee Volume of the Society of Biology of Paris in 1899 (*Cinquantenaire de la Société de biologie, Vol. Jubilaire,* p. 360, 1899), and made an interesting contribution to my journal (*Teratologia,* ii. 245, 1895) on the etiological relations of sterility, monstrosities, abortion, mortinatality, delayed development, and congenital debility. His experiments may be divided into three groups, with two only of which we have now to do. The third group deals with the production of teratomata by embryonic grafts. The first group contained those in which the conditions external to the egg were altered: Féré, here, repeated many of the experiments of Dareste and others, with alterations of temperature, traumatism, mechanical vibrations, white and coloured light, and varnishing; but he carried out on a large scale a series of check or control experiments, and he was careful to allow the eggs to remain at rest in the dark before beginning any experiments with them. Further, he tried the effect of gases which might penetrate the shell; thus he surrounded the eggs with an atmosphere of turpentine, musk, mercury, phosphorus, ammonia, ether, chloroform, alcohol, and tobacco before submitting them to incubation. No eggs were used of an age greater than eight days from the time of laying. The second group of experiments contained those in which substances in solution were injected into the albumen of the egg; in this way Féré tested solutions of salt, glucose, glycerine, iodide of potassium, bromides of potassium and strontium, peptone, creatine, xanthocreatinine, cantharidine, nicotine, sulphate of strychnine, hydrocyanic acid, various alcohols and essences, acetone, microbic toxines, blood, morphine, sulphate of atropine, hydrochlorate of cocaine, and venine. In this group, also, rigid control or check experiments were always carried out, and large numbers of eggs were used.

The results of Féré's experimental work were very striking. He found, for instance, that there was a direct relation between the teratogenic and the toxic power of poisons; this was well borne out in connection with the alcohols, and the following table of results shows that those which were most toxic were also most teratogenic.

FÉRÉ'S EXPERIMENTS ON THE TERATOGENIC POWER OF THE ALCOHOLS.

First Series.

No. of Eggs.	Nature of Injection.	Proportion for 100 Embryos.		
		Normal.	Non-developed.	Monstrous.
12	Controls . . .	66·66	25·00	8·34
45	Ethylic alcohol . .	68·68	13·33	17·79
22	Propylic ,, . .	40·90	4·54	54·56
23	Isopropylic ,, . .	8·69	8·69	82·62
21	Butylic ,, . .	47·63	0·00	52·37
11	Isobutylic ,, . .	27·27	9·09	63·64
22	Amylic ,, . .	4·54	27·27	68·19
10	Isoamylic ,, . .	10·00	10·00	80·00
	Second Series.			
24	Water	75·00	16·66	8·34
63	Ethylic alcoholic . .	53·96	11·11	34·93
63	Methylic ,, . .	23·80	11·11	65·09

Further, the microbic toxines that are most deadly for the hen are also the most deadly for the embryo chick, and inversely. Morphine, for instance, which is well borne even in large doses by the fowl, may also be injected in large doses into the egg without hurting the embryo. The same is true of cocaine and atropine. Generally, the agents which determine anomalies of development produce at the same time a marked retardation of growth, so that it may be said that the anomaly is in relation with the retardation of growth. Dwarfs were frequent in all the conditions in which anomalies were common. Some substances which had a dystrophic effect in large doses had a eutrophic effect in small ones; but in estimating such differences it was always well to bear in mind the individuality of the germ, so strongly insisted upon by Dareste as well as by Féré. Even in the case of prussic acid (of enormous teratogenic power) some of the embryos escape. This individuality is, of course, manifest in the human subject in relation to various infections, etc., where it may take the form of sporadic immunity. Further, Féré sometimes found among a lot of eggs which had been subjected to a teratogenic influence, and most of which had in consequence been arrested in development or malformed, one egg with a development not simply normal but above the normal. This occurrence indicated a tendency to variation, which, according to the dose of the agent and the individual trophic equation of the germ, might appear either in the direction of exaltation or in that of depression. There might then be, so to say, supra-anomalies as well as infra-anomalies. The same phenomenon was met with in families of human beings in which men of genius existed side by side with vicious and intellectually degraded individuals. During the past two or three years Féré has specially experimented with substances such as caffeine which might be supposed to have a stimulating effect upon embryonic development and growth, and has found that with small doses there is some evidence of such an action. The same was true of antipyrine.

Féré noted, also, that, while the number and gravity of the defects of development increased with the intensity and the duration of action of the disturbing causes, no particular monstrosity was related to any special influence. This fact, of course, had been previously observed by Dareste. It was also noted that a physical or chemical agent which had a teratogenic action when the organism was in the embryonic stage had a pathogenic action at a later date; and as was pointed out in the article in *Teratologia* (referred to above), the same influence might, according to the time when it acted, cause sterility, monstrosities, abortion, morti-natality, retarded growth, or congenital debility.

Féré, in strong contrast with Dareste, paid little attention to the monstrosities he succeeded in producing, and dwelt rather on the causes and their nature. At the same time he was always careful to enumerate the results of his experiments: in many cases there was absence of development or blastoderms without embryos; in many others there was cyclopia, or dropsy, or heterotaxy, or doubleness of the heart, or omphalocephaly, or atrophy of the head.

I may here refer very briefly to some experimental work done by other observers. Maffucci (*Centrlbl. f. allg. Path. u. path. Anat.*, v. 1, 1894; *Ann. Surg.*, xx. 385, 1894; *Policlinico*, i. 33, 1894) investigated the effect of pathogenic germs on the hen's egg and fœtal rabbit, and found that while the embryo lived, pathogenic germs did not develop in its tissues except in rare circumstances; they might, however, be stored up for later development in extra-ovular life. S. Kaestner (*Arch. f. Anat. u. Entwcklngsgesch.*, 319, 1895; *Verhandl. d. anat. Gesellsch.*, Jena, x. 136, 1896) made experiments by cutting off the artificial heat for a longer or shorter time during the incubation of hens' eggs; he thought the malformations which followed (*e.g.* arrest of development of head, defect in area vasculosa) were due to the cooling of the yellow yolk which caused the embryo to be pressed against the vitelline membrane. P. Mitrophanow (*Arch. f. Entwicklngsmechn. d. Organ.*, vi. 104, 1897) tried the effect of varnishing one side of the egg before incubation; at ordinary temperatures he got no results, but if the heat was increased the area pellucida had an irregular shape, and there was delay in the formation of the primitive groove.

Féré has, to my mind, greatly advanced the science of experimental teratogeny by breaking down the dividing wall between it and general pathology, a dividing wall which was felt to exist in consequence of the peculiar nature of the supposed exciting causes of monstrosities (*e.g.* shaking, raising or lowering the temperature, varnishing, and wounding). Doubtless these might be the causes of diseases as well as of monstrosities; but it was difficult to imagine them in action in the case of mammals, and more particularly in the human subject. Féré, however, at once broke down this wall when he introduced such substances into the egg as alcohol, morphine, strychnine, nicotine, and microbic toxines; these were already known to be the causes of disease, and the results of Féré's experiments showed them to be also teratogenic. Immediately, it was seen that experimental teratogeny fell into line with experimental pathology; the experimentalist felt that here he was dealing with similar things. The results might be very different—monstrosities as a matter of fact were very different from diseases—but it was possible to consider that the differences were due, not to variations in the cause, but to dissimilarity in the structures acted upon, namely, immature organs as compared with mature ones. The causes then might be similar but the effects different. Another good result followed Féré's work: it gave to teratogeny a clinical aspect. If the causes of disease were likewise the causes of monstrosity, then it might be expected that in the parents, and especially in the mother of malformed fœtuses, some trace of such morbid causes might be found. The question then arose whether malformed offspring were more common in the case of alcoholic parents or of those suffering from syphilis, tubercle, infectious fevers, and the like. That question cannot be said to be fully answered yet, but it is in process of being answered (as the reader will find demonstrated in the first section of this Manual, under such headings as fœtal syphilis, fœtal tubercle, fœtal alcoholism), and so far there has been not a little supporting evidence drawn out of the facts.

Let us now return from this long excursus into the realm of experimental teratogeny. It was made, the reader will remember, in order to ascertain whether experiment had any answer to give to the question of the cause of amniotic arrest or disease. It was regarded as highly probable that defect of the amnion, acting by pressure, was the cause of the arrested development of the embryo, which in its turn produced the malformation or monstrosity; but the further question was raised, What was the cause of the amniotic defect? Dareste's experiments increased our knowledge of the mode of action of amniotic defects, but did not give any utilisable information as to the causes of them. Féré's researches, however, showed us that probably the causes of disease are just the causes of the malformations. But now we have to inquire whether we can link together the results of Dareste's and Féré's work, and conclude that the imperfect development of the amnion is the cause of teratological states, and that the causes of disease are the causes of the imperfect development of the amnion. Here a surprise awaits us, for Féré seems, more especially in his recent writings, to be taking up a position antagonistic to the amniotic theory. In his "Note sur l'embryotomie tératologique" (*Rev. de chir.*, xx. 592, 1900) he criticises the idea of the teratogenic effect of amniotic pressure, and points out that Dareste himself had found in some cases that the amnion was widely separated from the embryo by a copious supply of liquor amnii, and that the same anomalies may occur both with and without arrest in the development of the amnion. By varnishing a longitudinal half of the egg, Féré succeeded in obtaining an embryo in which the head was separate from the trunk, and yet the amnion formed a large ovoid sac whose walls were far removed from the embryo. In another egg, which had been subjected to the influence of xylol fumes during incubation, Féré discovered an embryo with deformed cephalic and caudal parts joined by a narrow neck of constriction; yet the amnion formed a broad sac at the point of constriction. The conclusion which Féré draws (and he is apparently warranted in doing so) is that the amnion is not necessarily the means by which ontogenesis is arrested and malformations produced. He seems to suggest that in the place of the amniotic factor we must put a change in nutrition. The reader may feel (and he is justified in so feeling) that, after all, experimental teratogeny has not done much for the understanding of the mode of origin of monstrosities if it has weakened a belief in the influence of the amnion. It may be said that the same cause may be active in producing both the embryonic malformation and the amniotic defect, and that that cause may be a disturbance of nutrition due to toxic or microbic influences; but I am not sure that this generalisation makes up in value for the loss of the amniotic theory which it seems to entail. Further, we still await clinical confirmation of the hypothesis that germs and their toxines and inorganic and organic poisons acting on the parents produce malformed offspring. Personally, I am loath to throw overboard the theory of amniotic influence in teratogenesis, and to welcome in its place the hypothesis suggested by Féré; but it seems to me that it is not impossible to combine the two, and to believe that, as the human amnion apparently precedes the human embryo in the date of its development, so a general defect of nutrition may arrest the growth of the former and by pressure lead to arrest of the ontogeny of the latter. When the amnion is not arrested and the embryo is nevertheless malformed, it is permissible, I think, to imagine that the general cause (nutritional or other) came into action after the amnion had been formed and acted in some other (non-amniotic) way upon the embryo. The explanation is not in all points satisfactory, but it in some measure fits the facts as we find them. At the same time it may be repeated that the way is not yet closed against the advance of new hypotheses which may still better fit the facts.

Now it is quite time that I refer to the third strand in the Ariadne-thread that is leading us through this labyrinth of hypotheses, suggestions, and (it is feared) imaginings concerning teratogenesis. The reader may by this time be in grave doubt as to the reliability of the Ariadne-thread to lead him out of the labyrinth; he may suspect that he is only being led more deeply and hopelessly into its perplexingly intricate and anfractuous passages. Further, he may be reminding himself that the writer has as yet advanced no explanation at all for the occurrence of double monsters and malformations by excess, and that the hereditary transmission of special malformations from parent to child has in no way been dealt with. Obviously, neither amniotic pressure nor nutritional defects offer a reasonable or satisfactory explanation of these problems. The writer informs the reader that these problems are precisely the ones which he is now to take up, and that it is for their elucidation that he presents the third strand of his Ariadne-thread. May it be strong, and may it lead us out of this gloomy labyrinth, and that quickly.

We have already seen that some of the morbid states found existing in the fœtal period of antenatal life had their cause and origin in the embryonic; similarly there is good reason to believe that some of the more peculiarly embryonic conditions, such, for instance, as the double monsters, may originate in the pre-embryonic or germinal epoch. In introducing the germinal factor into the explanation of certain monstrosities, I am not trying to get out of an impossible position by referring a difficulty, which is inexplicable by any known mechanism in the little understood embryonic period, back into the less understood germinal period. There are some facts to go upon, albeit they are neither numerous nor completely established; perhaps they ought to be called quasi-facts. There are certain purely physiological conditions which are apparently determined in the pre-embryonic stage of antenatal life. For instance, when a child inherits peculiarities and characteristics from his father, these must have been impressed on the germ prior to the appearance of the embryo in the embryonic area; they must, indeed, have existed potentially in the spermatozoon before impregnation. Again, there is good reason to believe in the determination of sex prior to the embryonic epoch, and to accept the statement that the ova are already male or female, although, in the case of the higher animals, there are no discoverable structural differences which shall tell us to which sex they belong. This, at any rate, is the belief of M. von Lenhossék (*Das Problem der geschlechtsbestimmenden Ursachen*, Jena, 1903) and several others. It must be admitted, however, that some, *e.g.* A. van Lint (*Qu'est-ce qui determine le sexe?* Paris, 1902), are of opinion that the sexual future of the offspring is not settled till impregnation, and that when a "strong" spermatozoon meets a "weak" ovum the embryo will be female, and *vice versâ*. This does not, however affect the main question, for impregnation takes place in the germinal or pre-embryonic epoch.

When we pass from physiological to pathological states, we are almost compelled to admit that some of them, like the sex of the embryo, and like some of the hereditarily transmitted paternal traits of character, must be determined in the germinal period of antenatal existence. Thus when we meet with the same malformation in two or three generations of the same family, there seems no other reasonable explanation of the occurrence than that either in the spermatozoon or in the ovum there was a teratogenic something which determined the abnormal development of the embryo. There is no lack of instances of such occurrences, as, for example, hereditary hare-lip, fistulæ in the lower lip, aniridia, coloboma of the iris, microphthalmia, fistula auris, ectromely, ectrodactyly, polydactyly, polymastia, absence of the patella, hypospadias, etc. etc. The occurrence, also, of the same malformation in several members of the same family seems to require a similar explanation.

Then there is the question of the causation of twins, binovular and uniovular, and of double monsters. Twinning would seem clearly to be a state determined by the existence of several ripening ovi-sacs in the ovary at the same time, or by anomalies in the ova (or spermatozoa) before or during impregnation. Double terata, likewise, may be explained by the entrance of two spermatozoa into one ovum (polyspermy), or, perhaps, by the presence of two germinal vesicles in one ovum. I cannot, at this point, enter into the consideration of the evidence in favour of these views,—that will come in its proper place in the chapters treating of germinal pathology,—but it may be said that it is largely of the experimental kind. There has been accumulated, of recent years, much evidence founded upon experiments carried out upon the ova of various animals (especially echinoderms and ascidians), with which the names of such well-known experimenters as Chabry, Roux, Driesch, Hertwig, E. B. Wilson, and others, have been connected. These will be referred to by and by; in the meantime it may be taken for granted that there is proof that altered surrounding conditions may seriously affect the future of the ova subjected to them, and that, not infrequently, teratological results follow. The altered surrounding conditions may be due to chemical substances or toxines, or to mechanical agencies, and thus the causes of germinal pathology may be brought into line with those active in embryonic, fœtal, and postnatal pathology; the causes may be the same while the effects are various.

The germinal factor, then, is the third causal state which is advanced to clear up the origin of monstrosities. In it may be found the explanation of diplogenesis (or the formation of twins), of diploteratology (or double monsters), and of the hereditary character of malformations in certain families. I have done little more, at this stage, than indicate its nature; its full consideration must be reserved till germinal pathology is dealt with.

Summary.

To gather up all these threads of argument and proof, let me very briefly summarise what I believe are the chief causes of monstrosities. They are the results of disorderly embryology, of disturbed ontogenesis and organogenesis. Many of them are arrested developments, and represent stages which ought to have been temporary in ontogenesis, but which have remained stationary while other and neighbouring parts were pursuing the path of normal development. In the case of some of them at least the amnion would seem to act by pressure, and so delay, or altogether stop, the progress of events in ontogenesis. The amniotic influence, in its turn, may be the result of the action of toxines, poisons, and mechanical states which delay the formation of the amnion; or possibly these substances and states may act directly upon the embryo and alter its nutrition, and consequently its development and growth. Other monstrosities, and more particularly those by excess and the double terata, may be due to morbid causes acting upon the blastoderm before embryonic life begins, or upon the ova and spermatozoa before or during impregnation. On the other hand, there are minor monstrosities or malformations which may, perhaps, be produced in the fœtal period by the action of intra-uterine pressure or external traumatism; for it must be remembered that certain parts of the organism are still in the formative or embryonic stage, although the organism, as a whole, has passed into the fœtal phase. Finally, it is not impossible that the same ultimate causes may be active in all the three periods of antenatal life, although the results are so strikingly different.

In all this, there is much that is uncertain, obscure, dark; but perhaps

> "A Light
> Will struggle through these thronging words at last."

CHAPTER XIII

Classification of Teratology: Historical Sketch of the Systems of Empedocles, Obsequens, Lycosthenes, St. Isidore, Weinrichius, Schenkius, Aldrovandus, Licetus, Huber, Haller, Buffon, Malacarne, Penada, Meckel, Breschet, Charvet, Saint-Hilaire, Gurlt, Otto, Bischoff, Sangalli, Förster, Davaine, Billard, Ahlfeld, Cleland, Hirst and Piersol, and Thompson Lowne; Difficulties of Teratological Taxonomy; "Connecting Links"; Taruffi's System of Classification; Teratological Nomenclature; the Author's Classification based upon Taruffi's; Special Teratology of Embryonic Life, and of Germinal.

It may be stated with some assurance that many investigators have been turned from the study of Teratology by the complexities of its various schemes of classification and the eccentricities of its nomenclature. The subject has suffered and is suffering from too much classification, and from too many names of too many syllables. The science of monstrosities is not ready for any permanent mode of classification; neither, it will be remembered, was that of the pathology of the fœtus (*vide Manual of Antenatal Pathology—The Fœtus*, p. 174). Teratology, however, deals with matters much less easy to distribute or arrange systematically than does Fœtal Pathology; its classification, therefore, although much attempted, is in a still less satisfactory state than that of Fœtal Pathology.

The primary requisite of classification is that the facts or phenomena should all be known, and this knowledge cannot be postulated for Teratology. The object of such Taxonomy is to bring together those things which most resemble each other, and to separate those which differ; and this object, on account of our want of knowledge of the facts, cannot be attained in connection with Teratology. It is necessary, however, that there be some sort of grouping, tabulating, collocating, or disposing of the facts, such as are known, even if for no other purpose than to serve as an aid to memory, a *memoria technica*. This object may be attained in several ways, but to my mind the best, because the simplest, plan is a regional arrangement, such as I adopted in *Teratologia* in 1894, and have employed ever since. It is modelled upon Taruffi's scheme, used by him in his large work, *Storia della teratologia*, and differs from it only in details. Before, however, I give a sketch of this plan of classification, I must refer briefly to other methods which have, from time to time, been advocated by well-known teratologists.

In early times little or no classification of monstrosities was attempted. In the Chaldean cuneiform tablets dealing with monsters (Fig. 21, p. 89), the only scheme of arrangement would seem to be into those monstrosities that were born to ordinary people and those forming the offspring of royal parents; those who are interested in such matters will find a description of the different types in my article on the "Teratological Records of Chaldea" (*Teratologia*, i. 127, 1894). Empedocles, recognising in the male semen the great cause of generation in general, and of monstrosities in particular, found in it six conditions which might provoke teratological developments, namely, abundance of semen, defect, slowness, aberration of movement, and division of its substance; but it would be difficult to work out such an etiological classification nowadays, and we may well suppose it was no easier in the times of Empedocles and Aristotle.

When, in the Dark Ages, the supernatural origin of monstrosities came to be believed in, no classification in the real sense of the word was any longer possible. Julius Obsequens in his *Prodigiorum Liber* simply allocated the monstrosities known to him according to the year after the founding of Rome in which they were born; Conrad Lycosthenes, in his larger *Chronicon Prodigiorum atque Ostentorum* (1557) pursued the same chronological plan, but enlarged its scope "ab exordio mundi usque ad nostra tempora." Both these writers included marvellous occurrences as well as human monstrosities in their works; so it comes about that we find the plagues of Egypt, earthquakes, and one-eyed infants placed side by side in their attractive and surprising pages.

The first attempt towards an arrangement of monstrosities having any classificational value seems to have been that of St. Isidore, the archbishop of Seville, in his work on *Etymologies* (600 to 636 A.D.). He placed them in ten groups, with, to distinguish them, such leading characters as large or small size, defect of parts, transformation of parts (*e.g.* the minotaur) or of the whole body (as when a woman gives birth to a calf!), transposition of parts, adhesion of them, precocious or delayed appearance of structures (*e.g.* teeth and hair), mixture of the sexes, and the presence of several different deformities in one case. There was no place found for the double terata. The Isidorian system is memorable; but it was disfigured by remnants of superstitious beliefs, such as the possibility of animal births occurring in the human subject. It was in advance of the systems which prevailed about the middle of the sixteenth century, when Lycosthenes was bringing out his *Chronicon*, and when Jandunius (1543) was referring monstrosities to defect, absence, excess, or activity of the menses or *materia.* There was, in fact, nothing so good as the Isidorian arrangement till the seventeenth century, for all sorts of fabulous monsters were believed in, and many diseases, such as elephantiasis, were grouped with the truly teratological states. Weinrichius (*De ortu monstrorum commentarius*, 1595) used some of Isidore's divisions; but he was, as Haller described him, a credulous man and not an anatomist.

The Schenks, father and son, in their *Observationum medicarum, rararum, novarum, admirabilium et monstrosarum volumen* (Francofurti, 1609) introduced the idea of a regional classification of deformities; but their work was concerned with all sorts of matters besides monstrosities; and the first to use this method of arrangement for teratological phenomena alone was Ambrosinus in his edition of the works of Ulysses Aldrovandus (1642). Under the head of monstrosities Aldrovandus included the anomalies of animals and plants, and so was the founder of the science of Comparative Teratology, which is only now beginning to take its place with Human Teratology in the larger subject of Anomalous Formations. First the deformities of the head were dealt with, then those of the arms, hands, abdomen, genitals, and feet, then those of the skin and of the tail (in animals), then dwarfs; and finally double monsters were described.

There is much to be said in favour of a regional classification of monsters in the present imperfect state of our knowledge, and I have adopted it as the basis of the arrangement used in this work; but the system of Aldrovandus (with Ambrosinus as his editor) was not elastic enough to include all true malformations, while, on the other hand, it provided places for fabulous creatures which ought to have been closely scrutinised before they gained admittance within the limits of the subject. Licetus also, in his treatise *De Monstris* (1616), would have been wise had he been more sceptical regarding the genuine character of many of the curious hybrid productions which he pictured and placed among the multiform monsters of his classification. He divided all monstrosities into the multiform and the uniform: among the former he placed the monsters made up of the parts of animals of different species or of different individuals of the same species, including the centaur, the minotaur, the infant with a bird's wings, and diablotins; while among the latter were human or animal monstrosities of the mutilated type, or with superfluous parts, or of doubtful sex, deformed, formless, and "enormous." There are details in the scheme of Licetus which remind us of St. Isidore's classification; but Licetus lays no great stress upon arrangement, and was more occupied with the enumeration of causes.

No new plan of teratological classification made its appearance during the hundred years that followed the publication of the work of Licetus; but in 1748 J. J. Huber (*Observationes atque cogitationes nonnullæ de monstris*) distinguished nine classes of monstrosities, among which were the well-established types of excess or defect of development, along with such novel varieties as "union of parts usually separate" and the "closed state of canals usually open." Fabbri (*De humano quodam monstro*, 1767), as Taruffi states, added another type of monstrosity to those already known, namely, that due to a morbid process; but it was not till the time of Haller was reached that Teratology began to be scientifically defined, and, therefore, to be capable of scientific attempts at classification. Haller himself in his work *De monstris* (*Opera minora*, iii., 1768) was not particularly happy in his classification, for he employed different plans, and so missed uniformity; but he did much to rid the subject of the mediæval superstitions still adhering closely to it, and so earned the gratitude of future generations of teratologists. Buffon's division of monstrosities into those by defect of development, those by excess, and those by altered relation of parts, was not so much a classification as a conception of the ulterior etiology of teratological phenomena in general. It was an attempt, after the manner of Empedocles, to introduce Teleology into Teratology, and to discuss the final causes of things. Some twenty years after Buffon's *Histoire naturelle* appeared, V. Malacarne (*Mem. della soc. ital.*, ix. 49, 1798) published a scheme of classification with many classes so as to offer a place for all known monstrosities; but although he did not succeed altogether in this aim, he was happy in his construction of the names of teratological types from Greek roots, and the words microsomia, macrosomia, micromelia, macromelia, and polymelia suggested by him have been retained by several modern writers and classifiers. Some of Malacarne's classes, as those for men with limbs of animals and for animals with human extremities, were ridiculous.

The nineteenth century saw a great development of the taxonomy of Teratology, although it may be doubted whether much of the time spent upon it might not have been better employed. In the early years of the century J. Penada (*Atti dell'Accad. ital. d. sc.*, I. pt. i. 284, 1810) tried to get back to the more general aspects of Teratology, and proposed to divide monstrosities into three groups according to the proximate causes, which he found in anomalies existing in the germ, in external and mechanical conditions affecting the fœtus, and in diseases, such as dropsy, attacking the unborn infant. Although there was much that was far-seeing and thoughtful in Penada's scheme, it was not, at the time when it was published, capable of being utilised for the purposes of classification. J. F. Meckel, with less originality than Penada but with more immediate advantage, adopted Buffon's division of malformations into three causal sections (1, diminished formative force or energy; 2, increased formative force; 3, anomalies in form and position of parts), and added thereto a fourth containing the hermaphrodites. Meckel worked out the details of his scheme with wonderful completeness (*Handbuch der pathologischen Anatomie*, Bd. I., II., Lipsiæ, 1812–16), but with no little difficulty and with many somewhat forcible disjunctions of similar things and conjunctions of dissimilar things. His group of hermaphrodites, also, did not fall into line with the other three divisions, and stood rather awkwardly by itself. The classification proposed by Breschet (*Dict. de méd.*, vi. 524) got over one of these difficulties by giving no separate place to the hermaphrodites; the third division (anomalies in form and position of parts) was also done away with; and, under names derived from the Greek, four orders of teratological processes were enumerated, namely, agenesis, hypergenesis, diplogenesis, and heterogenesis. The first two of these processes corresponded to the old divisions of monstrosities by defect and excess; the third process was that which produced double terata; while the fourth gave origin to a group containing an extraordinary medley of formations, including twins, ectopic pregnancy, albinism, and cyanopathy. Breschet gave to double monsters a place among four orders; but Charvet (*Recherches pour servir à l'histoire générale de la monstruosité*, Paris, 1827) divided all anomalies and monstrosities into two large classes, one of which contained the double terata, and the other the single ones (deformed by irregularity, by defect, and by excess).

We come now, in chronological order, to the classification elaborated by the Saint-Hilaires (Etienne and Isidore), by far the most complete and thorough that had yet appeared. These writers, in their works (*Philosophie anatomique*, ii. 1822; *Histoire des anomalies*, vols. i., ii., iii., 1832–37) built up nothing less than a great edifice, a huge classificational structure, providing accommodation for all the then known types of anomaly, and dwarfing all other competitive fabrics as well by its bulk as by its intricacy. The idea adopted and worked out by the Saint-Hilaires was similar to the natural method of classifying plants and animals; in fact anomalies were regarded as constituting a "Kingdom." This kingdom was divided into four primary divisions: there was, first, the division of the hemiterata or simple anomalies, malformations which did not profoundly influence the whole organism; there were, second, the heterotaxies, the internal anomalies which did not affect any functions, and found their typical state in situs inversus or transposition of the viscera; there were, third, the sex anomalies, grouped together as the hermaphrodisms; and there were, fourth, the monstrosities, which included internal and external defects of a marked kind. Thus far the classification did not differ greatly from some others; but the Saint-Hilaires subdivided these four main branches or divisions in a most complicated manner into classes, orders, tribes, families, and genera. For instance, the monstrosities were divided into two classes—the single monsters and the composite or double (and triple) monsters; to take again the single monsters, they were divided into three orders, that of the autosites, that of the omphalosites, and that of the parasites; then the autosites were divided into four tribes, and these tribes were divided into two or three families each; and, finally, each of these families, *e.g.* that of the ectromelians, was divided into several genera. The hemiterata were split up, although not with such complexity, into similar groups; while the heterotaxies and hermaphrodisms had a much simpler arrangement. The scheme of classification of the Saint-Hilaires by its very completeness lays itself open to criticism. Its most serious fault, however, is found in the primary conception that anomalous creatures form a world by themselves, a great kingdom or sub-kingdom like that of the plants or the animals; there is no justification for such a comparison. Further, the idea of genera, species, and the like, which arises out of this conception, leads to the use of these expressions in a very misleading sense; for while species in Zoology are groups of living beings which transmit by generation a complex of characters, species in Teratology are simply individuals suffering from the same malformation. We can, however, use the classification without accepting the ideas of species, genera, and families which underlie; we may simply look upon these as larger and smaller divisions not related to each other in the intimate way suggested by the Saint-Hilaires. The nomenclature is in many respects admirable; it is mainly formed upon Greek roots; and, what is greatly in its favour, it has been largely accepted not only in France but also in other countries.

In the hands of E. F. Gurlt, Comparative Teratology was fashioned into a science. The classification which he employed (*Lehrbuch der pathologischen Anatomie der Haus-Säugethiere*, ii., 1832) was comparatively simple. He divided all monstrosities into two classes: the first contained the simple or single monsters; the second, the double terata and the very rare triple monsters. He had, also, a third group in which were the anomalies of individual organs of the body. In his first class were to be found monsters by defect (*monstra per defectum*), by smallness of parts (*parvitas partium*), by division of the body (*fissio corporis abnormis*), by union of parts (*coalitio partium*), by contortion, and by excess (*per excessum*); and he placed with all these the hermaphrodites. The difficulties of separating the single monstrosities rigidly from the anomalies of individual parts were too great to be overcome by any scheme, and as a matter of fact they were not overcome by Gurlt's arrangement. Further, it is an anomaly for cases of *fœtus in fœtu* to appear anywhere save among the double terata; Gurlt has placed them in the third group.

Otto's classification (*Monstrorum Sexcentorum Descriptio Anatomica*, 1841) pursued the now beaten track of division into two classes, *monstra deficientia* and *monstra abundantia*; but to these two a third class was added of *monstra sensu strictiore deformia*, which contained spina bifida, facial fissures, exomphalos, ectopia vesicæ, syndactyly, and deforming diseases (*e.g.* hydrocephalus, congenital rickets, dropsy, cysts, and tumours). Otto's collection included both human and animal monstrosities. His third group was an awkward one, containing as it did anomalies in no way resembling each other.

T. L. W. von Bischoff (in R. Wagner's *Handwörterbuch der Physiologie*, i. 901, 1842) gave a classification of much the same kind: he had three primary divisions into monsters by defect, by excess, and by alteration of form without either excess or defect. He placed malformation due to atresia or to fissure in the first group, double monsters in the second, and hermaphrodites in the third; but he also placed the amorphous, acormic, and acephalic twin fœtuses in the first group. Every classification founded upon the distinction of defective and excessive development broke down in one or other of its details; and Sangalli in 1860 (in an article quoted by Taruffi, *Storia della teratologia*, i. 366, 1881) did not greatly diminish the difficulty by having five primary divisions (excess, defect, anomaly of position, abnormal division, and abnormal union).

A. Förster's contributions to teratological taxonomy deserve a paragraph to themselves. At first, in his work *Die Missbildungen des Menschen*, published in 1861, he adopted the usual plan of dividing monstrosities into those by excess, those by defect, and those "per fabricam alienam," or *monstra abundantia, deficientia, et alienantia s. aberrantia*; but in a later book (*Handbuch der pathologischen Anatomie*, ii., 1862–65) he tried to arrange teratological formations according to the time in antenatal life when they were supposed to originate. In one group he placed the results of the pathological development of the germinal area, including pathological twin states (double monsters and placental parasites), pathological development as regards size (giants and dwarfs), and heterotaxy; in a second group were the pathological developmental states of the extremities (excess or defect); in a third were those due to abnormal development of the spinal canal; while in the fourth, fifth, sixth, seventh, and eighth were those resulting from anomalies in the ontogenesis of the face, neck, thorax, abdomen, intestines, uro-genital organs, and vascular system. This plan was scientifically sound, and it will yet, I believe, be accepted; but, at the time when Förster wrote, the details of organogenesis were not well enough known to permit of the application of such a time-arrangement of monstrosities. Even now, with all our additional knowledge of early antenatal affairs, it is doubtful whether we can assign the various monstrosities to their special dates of origin. F. v. Winckel, however, has applied the principle very satisfactorily to uterine malformations (*Ueber die Eintheilung, Entstehung, und Benennung der Bildungshemmungen der weiblichen Sexualorgane*, Leipzig, 1899); although, of course, these anomalies, on account of the late date when the genitals develop, are more easily traced out and allocated to the proper weeks. For one great generalisation we are much indebted to Förster, namely, that Teratology is the Pathology of the Embryo; a great clarification of teratological problems has resulted therefrom, although many things yet remain dark, as the reader knows very well by this time.

C. Davaine in his article "Monstres" in the *Dictionnaire encyclopédique des sciences médicales* (2nd Series, vol. ix. p. 260, 1875) struck out a new line in the classification which he followed. He divided monstrosities into two divisions according as the anomalies affected organs concerned in the life of the individual or parts devoted to the reproduction of the species. Obviously the divisions were of very unequal size, even although Davaine put the double terata into the second one. As a classification little is to be said in its favour; indeed, its utility is less than that of the plan of C. M. Billard (*Traité des maladies des enfans*, p. 399, 1835), according to which all congenital diseases and malformations were divided into three groups according as they were necessarily fatal to life, or were opposed to the development of an independent existence, or were no obstacle to viability.

F. Ahlfeld (*Die Missbildungen des Menschen*, Parts I. and II., 1880–1882) in the two parts of his work which have appeared, deals with double monsters, anomalies by excess of individual parts, and giant growths in one division ("Spaltung, Doppelbildung, Verdoppelung"), while in another ("Spaltbildung") he considered all the malformations characterised by fissure-formation and patency of openings which ought to close. The second group, in particular, contained a medley of anomalies with no very strong resemblance to each other to hold them together in taxonomic order. J. Cleland's classification (*Memoirs and Memoranda of Anatomy*, i. 131, 1889), being founded, as it is, upon causation, necessarily rests upon theories rather than on established facts and individual resemblances; but it contains much that is well worth consideration, and for that reason I reproduce it here in brief:

Monstrous and Anomalous Forms.

I. *By Defect*—
  A. Without distinct external cause.
    1. Dwarfing. 2. Failure of completion of form of parts.
  B. Consequent on dropsies and changes connected therewith.
    1. Pleuro-peritoneal. 2. Cerebro-spinal.
  C. By Strangulation.
    1. By thickened tissue occluding openings or preventing their formation.
    2. From obstruction to the separation and expansion of potential parts.
    3. From external causes, *e.g.* umbilical cord, and bands of fibrin.
II. *By Excess*—
  A. Hypertrophy.
    1. Of whole body—Giants. 2. Of parts.
  B. Multiplication of parts—Polydactylism.
  C. Longitudinal fission of embryonic mass.
    1. Complete fission.
      A. Permanent (twins in one chorion).
      B. Temporary (the divisions being subsequently united by corresponding parts).
    2. Incomplete fission.
      A. Abcaudal.
      B. Abcranial.
      C. Fission simultaneously abcaudal and abcranial.

B. Cooke Hirst and G. A. Piersol (*Human Monstrosities*, 1891), being dissatisfied with all the plans of classification which have been proposed, adopted that of the Saint-Hilaires as being founded on wide observation and possessing flexibility and familiarity. These authors, therefore, divided anomalies into the four groups of the hemiterata, the heterotaxies, the hermaphrodites, and the monsters or terata (proper); but they made slight modifications in the subdivisions, substituting, for instance, Förster's arrangement of double terata for that of Saint-Hilaire.

Thompson Lowne (*Descriptive Catalogue of the Teratological Series in the Museum of the Royal College of Surgeons of England*, 1893) adopted a regional classification as being that best suited for Museum work. In all, eleven series were enumerated, and several of the series were subdivided into anomalies by excess, by defect, and by distortion. The first series, that dealing with abnormal conditions affecting the head and trunk, was disproportionately large; it was divided into five classes (situs mutatus, secondary dichotomy, double malformations, malformation with deficiency, and malformations by distortion). Utility for referencing was the governing principle of the arrangement, and in that respect it achieved its purpose.

In the preceding historical sketch of the leading systems of classification that have from time to time been in use, I have tried rather to indicate the principles upon which each plan was founded, than to give complicated details of the way in which it worked out. I have passed from the chronological arrangements of the mediæval writers to the systems founded upon external characters, to those based upon causes or alleged causes, to those having a regional, a prognostic, or a medico-legal character, and to those in which the course of events in antenatal life was taken into account. The progress of Embryology, the advance of Fœtal Physiology, the discovery of undescribed types of monstrosity, and further researches upon already known types, have seldom failed to reveal the existence of defects in these classificational schemes, and have weakened their utility. The observation of connecting links between different types has been a specially fertile cause of rearrangements and reclassification. For instance, it might appear at first sight that a line could easily be drawn between double and single monsters, between, in other words, united twins and monstrosities in which only one fœtus is involved. Between the Siamese Twins and an anencephalic fœtus there is all the difference possible, for the one is so obviously two united individuals, and the other is nothing more than a single defective fœtus; but there are double monsters which show almost no external signs of duplicity at all. Perhaps the best instance of such is found in the newly established type (or genus, to use Saint-Hilaire's name) rhinodyme. P. Gilis (*Journ. de l'anat. et de la physiol.*, xxxv. 707, 1899) has described a case of this kind in the lamb. The body and neck were single, and at first sight the head also appeared to be so. There were two lateral eyes; but each maxilla, especially the lower, had a notch in the median line, and on examination of the deeper parts it was found that there were four nasal fossæ, four upper maxillæ of which the two internal ones were much reduced in size, two mandibles whose internal rami were fused posteriorly at the level of the angles, and two tongues fused behind in a single body attached to a single hyoid bone. There were then really two heads in this case, but they were not quite fused together. A similar case in the human subject was that described by Félix Regnault under the name of "La Femme à deux nez" (*Bull. et mém. Soc. d'anthrop. de Paris*, 5 s., ii. 333, 1901). In this woman the eyes were wide apart, the mouth was broad, there were six upper incisor teeth, and there were two (fused) noses of which the left had two nares. There was an osseous plate between the two noses, which represented two upper maxillæ fused together; and there was the rudiment of a median orbit.

Such cases as the above illustrate very well the disturbing effect of these intermediate varieties upon classifications; but they have at least served the useful purpose of demonstrating that in Teratology we have to do, not so much with a series of clearly differentiated types, as with an almost interminable number of kinds of monstrous forms related more or less intimately to each other, and shading off into each other by almost imperceptible degrees. To attempt to classify them by their characters is very much like trying to classify shades of colour: we can pick out leading types and arrange all the others according as they differ from or resemble them, but we shall soon find that it is impossible to translate this method of grouping into a linear series. Yet, as we have seen, this is what many teratologists have tried to do. Now, the classification must never dominate the science; it must always be subordinate to it. It is necessary to have some way of grouping together teratological cases, but the cases are of far more importance than the grouping of them.

It may be that ultimately it will be found possible to classify anomalies and monstrosities according to their causes or according to the time in antenatal life at which they are produced, and in this work we are feeling our way, as it were, towards some such arrangement; but this cannot be yet achieved. The classification which I have adopted, therefore, is founded upon the more manageable ideas of general characters and the regional distribution of malformations. It is, as I have said already, closely modelled upon that employed by Taruffi in his monumental work (*Storia della teratologia*, vols. i.–viii., 1881–94). It contains the ground principle of the division of teratological conditions into those with excess of formation, those with defect, and those with altered relation. By combining this way of looking at terata with the regional arrangement of the actual types, a fairly satisfactory working system of classification is obtained. It has, of necessity, its defects; but it has the great merit of elasticity, and in it a place can be found for practically all forms of malformation. If it be accepted simply as a means of convenience in grouping together various teratological productions, and not as a scientific setting forth of the pathological and etiological relations of these monstrosities to each other, it will, I believe, be found to serve its purpose well enough. It is to be remembered that it is not for a moment intended that the larger and smaller subdivisions stand to each other at all in the relation of orders, tribes, families, genera, and species. It is to be thought of rather as a series of spheres of types related in various degrees to each other, and coming into contact in various planes, so to say.

Before I present an abbreviated sketch of the scheme of classification which is to be employed, it may be well for me to deal very shortly with teratological nomenclature. It is unquestionable that teratological terms are uncouth and unfamiliar to the eye and ear of the English-speaking medical man. It is true that some of them are not only polysyllabic to an almost alarming degree, but are also etymological riddles, to be read only by a good Greek scholar. It would be easier for us to give the various monstrosities English names; thus, we might speak of a double-headed twin monster, or of a brainless fœtus, or of a one-eyed monstrosity. Such designations would be more easily understood by us than such names as dicephalus, anencephalus, monophthalmus, or cyclocephalus; but to scientists of other nationalities their meaning might not be plain. So it has come about that, for the sake of international convenience, Greek words have been made use of to found a teratological nomenclature. Scientists of all nations have, or ought to have, sufficient familiarity with Greek to be able to recognise the meaning of words built up upon Greek roots, and thus at the expense of a little trouble to each nation a general international advantage is gained. To the Englishman, "two-headed" may be more intelligible than "dicephalus," but it is not so to the Frenchman; while to educated Englishmen and Frenchmen alike, "dicephalus" conveys a very distinct and evident meaning. So it has come about that names derived from the Greek have been given to all the known types of monstrosity. To the beginner the nomenclature is difficult and confusing; but, after all, there are other departments of Science, and even of Medicine, that have a terminology every whit as difficult as that of Teratology: they are, however, more immediately practical or more generally studied, and their most polysyllabic terms have in consequence become more familiar to the eye and ear. At the same time it will be for the good of their science if teratologists will in the future refrain from the unnecessary coining of lengthy words to express slight differences in structure. In this work I shall use, as far as possible, terms derived from Greek roots.

Let me now give an outline of the plan of classification (a modification of Taruffi's) which I have adopted.

Terata (Monstrosities and Anomalies).

A. MONOSOMATOUS (a single individual involved).
    I. Pantosomatous (the anomaly affects the whole or nearly the whole body).
        (*a*) Dwarfism (microsomia).
        (*b*) Giantism (macrosomia).
        (*c*) Hemi-hypertrophy and Hemi-atrophy.
    II. Merosomatous (the anomaly affects only a part of the body).
        (*a*) Partial Macrosomia and Microsomia of various Parts.
        (*b*) Spinal Column and Contents, Anomalies of.
        (*c*) Cranium and Contents, Anomalies of.
        (*d*) Face and Sense Organs, Anomalies of.
        (*e*) Neck and Constituent Parts, Anomalies of.
        (*f*) Thorax and Contents, Anomalies of.
        (*g*) Abdomen and Pelvis and Contents, Anomalies of.
        (*h*) Limbs, Anomalies of.
        (*i*) Annexa (Placenta, Cord, Amnion), Anomalies of.
    III. Heterotaxic (the anomaly affects only the arrangement of the parts of the body).
B. POLYSOMATOUS (two (or more) individuals involved).
    I. Twins, entirely separate, but in a single chorion (monochorionic).
    II. Twins, united only by the vessels of their umbilical cords (omphalo- or allantoido-angiopagous).
        (*a*) Paracephalic.
        (*b*) Acephalic.
        (*c*) Amorphous.

III. Twins, united more or less completely (double monsters).
  (*a*) Symmetrically united—
    1. Syncephalic.
    2. Dicephalic.
    3. Thoracopagous.
  (*b*) Asymmetrically united—
    1. Cephalo-parasitic.
    2. Prosopo-parasitic.
    3. Trachelo-parasitic.
    4. Thoraco-parasitic.
    5. Gastro-parasitic.
    6. Lecano-parasitic.
    7. Melomelic.
IV. Triplets, Quadruplets, Quintuplets, etc.
  (*a*) Entirely separate.
  (*b*) United.
    1. By the vessels of the umbilical cords.
    2. Directly and more or less completely.

This scheme of classification requires little explanation. In it all teratological phenomena are divided into two great divisions; one, that of the monosomatous terata, in which only a single individual is affected; the other, that of the polysomatous terata, in which two individuals (or, at least, something more than one) are involved. Here, at once, it must be admitted that it is very difficult sometimes to allocate exactly every specimen to its proper place in one or other of these two divisions. The difficulty does not arise in respect to well-marked types, such as anencephaly or cyclopia and the Siamese Twins, but with regard to the intermediate types or connecting links, such as polydactyly or the diphallic monstrosity. An individual possessing no other signs of excessive formation than an extra digit or two penes instead of one does not at first sight show much resemblance to such a phenomenon as the Siamese Twins; but the reason is that they are on opposite sides of the sphere of types which has "excessive formation" as its one character. In the same fashion low types of animal life show little resemblance to the mammalia, and are at first sight more like plants; but they may be animals all the same. Of course, there are spurious signs of excessive development. A good instance of this is got in the so-called "double" uterus, which is, as every student of Embryology knows, simply an ununited or imperfectly united organ. These cases fall not under the polysomatous but under the monosomatous terata. The great majority, however, of cases showing excess of formation are grouped with the polysomatous terata, even although they exhibit somewhat scanty indications of their double nature.

The division of the monosomatous terata corresponds roughly with the two groups of "defects of development" and "altered relationship of parts." It includes the arrested developments and nearly all the conditions which have been called hemiterata or anomalies in the narrow sense of the word. The types are very numerous and have been subdivided according as the whole body is affected (pantosomatous) or only a part of it (merosomatous); and I have made a third division to hold the heterotaxies, the states in which the viscera are more or less accurately transposed. The only difficulty met with in this group arises with regard to the giants and hemihypertrophies. These are indeed "excessive," but the excess is apparently one of growth and not of development; and so they fall among the single monstrosities and not among the double. The subdivision of the merosomatous terata is the largest of all, and has had to be split up according to the region affected. A slight difficulty arises with the cases in which two or more parts of the body are simultaneously malformed, "connecting links" again playing havoc with the best laid plans of the taxonomist; but the difficulty may be surmounted by classifying the case according to its major malformation, and calling the minor ones complications, *e.g.* anencephaly, with its complications spina bifida and defects of the sympathetic nervous system. In turn, the spinal column, cranium, face, neck, thorax, abdomen, pelvis, and limbs are dealt with according as the anomaly affects one or other of them; and I have made a special group to contain the malformations of the fœtal annexa, including the placenta and funis, for they are as truly fœtal organs as are the liver and spleen, and their malformations have received little attention and deserve more. I have made no special subdivision for the hermaphrodites, but have placed them along with other malformations of the genital organs under the region of the pelvis. It is true that they have a peculiar importance on account of social difficulties to which they may give rise, and of the medico-legal questions which may emerge from their anomalous position; but to the antenatal pathologist they are simply cases of malformation of the genital organs. Most of them belong to the monosomatous terata, but it is possible that a few ought to be grouped with the polysomatous.

The polysomatous terata are subdivided into four groups. The first contains the monochorionic or uniovular twins. It is possible that here also ought to be placed the dichorionic or binovular twins, for twinning is an anomaly in the human subject; but the point is not pressed. It is on account of their twin-ship that monochorionic twins are included in this group; they need not necessarily exhibit any individual malformations. It is, however, a remarkable fact that twins often are malformed, one or both; and it is still more significant that they may exhibit identical malformations. In the second group of the polysomatous terata are the allantoido-angiopagous twins or placental parasites, those curious cases in which a very rudimentary fœtus is found existing in utero in a parasitic fashion, being attached to his co-twin by the vessels of his umbilical cord *viâ* the placental circulation. They are placed among the polysomatous terata because they are monochorionic twins in the first place, and on account of their malformed state in the second place; for it must be remembered that one of the twins may show no malformations at all, although there is reason to believe that from the standpoint of antenatal physiology he is seldom quite normal.

The third group of the polysomatous terata contains the double monsters or united twins commonly so-called. In them the union is between the two fœtuses and not by means of their annexa (membranes, cords, and funic vessels); and it contains such well-known types as the Siamese Twins, the Hungarian Sisters, the Scottish Brothers, and the like. It also includes the cases in which a rudimentary fœtus is inserted on to the other fœtus in a parasitic manner, as in the famous Laloo and in the Chinaman, Aké.

The fourth group of the polysomatous terata contains the plural pregnancies, in which more than twins are present in the uterus. With regard to triplets, quadruplets, quintuplets, and sextuplets (genuine cases of which in the human subject are very rare), there can be no doubt that their place is among teratological formations. Whether they show individual malformations or not, the very presence of three fœtuses in the human uterus at the same time is teratological. As a matter of fact, however, triplets, etc., are very often malformed. They may consist of two fairly normal fœtuses, and of a parasitic one attached to the placenta of one of the normal ones; in this case they are similar to the allantoido-angiopagous twins. In other, but exceedingly rare, cases three fœtuses may all be fused together leading to the production of a triple monster or united triplets.

Such is the scheme of classification which is used in this work. Its most serious defect is its overlapping, but this is unavoidable. It must also be remembered that on account of our defective knowledge of all the facts of our science, no perfect scheme of arrangement is at present possible; this classification, then, is not a scientific setting forth of the exact pathological and etiological relations of monstrosities to each other, but simply a convenient method of grouping them. We must not expect to introduce into our subject a mechanical "precision which has no counterpart in nature."

There is an interesting speculation connected with the classifying of monstrosities to which I have not yet referred; I mean the question whether we can separate the teratological conditions which arise in the embryonic period of antenatal life from those which are initiated in the germinal epoch. The reader who has perused the chapters dealing with Teratogenesis will be prepared for the statement that I think we can so separate teratological productions. I am of opinion that most of the monosomatous terata arise during the embryonic period, while the double terata are probably due to causes acting upon the organism in the germinal epoch before the first rudiments of the embryo can be recognised in the embryonic area. For this reason I shall describe the types of polysomatous terata under the Pathology of the Germ, along with deformities of the blastoderm and hydatid moles. I have found great difficulty in arriving at any conclusion regarding the position of congenital tumours: some of them, such as cysts of the neck and of the sacral and perineal regions, doubtless are formed during the embryonic epoch, and possibly also to some extent in the fœtal; but others, I think, must be regarded as germinal in origin. I shall, therefore, describe some of them with the types of embryonic pathology and others with those of germinal pathology. Teratology, then, includes more than the Pathology of the Embryo; it contains part also of the Pathology of the Germ. The Pathology of the Embryo and the Germ, on the other hand, includes more than Teratology; it contains morbid states which are not usually named teratological. I freely admit that there is much that is uncertain about this arrangement; but, as I have already said, we are only as yet feeling after some such grouping of anomalies according to the periods of antenatal life in which they originate.

I have now reached the end of what may be called the General Principles of the Pathology of the Embryo, and can, therefore, proceed to describe some of the leading types of the results of the action of morbid causes upon the new organism in the embryonic epoch. There is to be a long procession of such types, and it will be my purpose and my endeavour to give to the reader a clear, concise, and intelligible descriptive account of them as they pass by.

CHAPTER XIV

Teratological Types: The Types and their Bibliographies: Microsomia or Dwarfism; Growth Processes; Embryonic, Fœtal, and Postnatal Microsomia; Generalisations; Literature: Macrosomia or Giantism; Embryonic, Fœtal, and Postnatal; Literature: Unilateral Macrosomia or Hemi-hypertrophy: Unilateral Microsomia or Hemi-atrophy.

The teratological types form a long series, a very long series, as the reader will immediately perceive, if he have not already done so. We are now in a position to begin, with some profit, our study of these types. It may be that the reader has, long ere this, begun somewhat impatiently to look for some type-descriptions, and to marvel at their non-appearance. "So much time has been spent over general principles," he has been saying to himself with the suggestion of a grievance in his tones, "that there is little left for the actual description of the malformations and monstrosities themselves." And this is quite true if the present work is a catalogue of monstrosities; but, then, the writer ventures to hope that in some measure it is more than a teratological descriptive list. It is indeed put forth as an attempt to discover how there come to be monstrous formations at all, what the causes of teratological phenomena are, and how the prevention of such things is to be brought about. To arrive at conclusions on those matters, general principles, if we can get at them, are more likely to help us than are descriptions of individual types. No one surely wishes to retain the teratological types as a permanent possession of scientific medicine; there might well be rejoicing if there were any prospect of their being seen no more on this planet; like smallpox, they might happily be forgotten, were there but a similarly effective means of getting rid of them. We are not, of course, within measurable distance of any such consummation; but it is well to remember that the wished-for goal of this, as of all departments of the healing art, is prevention. We can at any rate look towards it. Meanwhile let us to the description of the teratological types.

It is obvious that there are types: the hasty survey of any collection of monstrosities suffices to make this plain. Further, some types are relatively commoner than others; and some are more clearly marked off from the rest than are others. Of the commoner and more clearly marked types I trust I may be able to paint fairly complete word-pictures; the rarer and less sharply delimited varieties of monstrosity will be indicated only by a few strokes, as it were, in outline, in black upon white. The former we may regard as full-length portraits, the latter as little more than vignettes.

The word "type" is used here in its simplest and most obvious sense; by it is meant only a "sort" or "kind" of monstrosity. Thus employed, it has neither ulterior significance nor specific meaning. It is no more than a conveniently short term to express an outstanding and fairly well delimited variety of monstrosity. The types, further, are taken up in the order of the system of classification sketched in the preceding chapter; but it is not suggested that they stand in any peculiar or vital relationship to the other members of the series in which they are placed. In other words, I do not give to the term "type" its common biological signification, for, as has been already explained, I do not regard Teratology as a "kingdom" in any sense resembling that of the plants or the animals.

Around each teratological type has grown up a bibliography, sometimes of considerable dimensions, and occasionally of enormous size. What to do with these lists of literature has been the subject of much thought. I have, in the past, put a high value upon such things, and there can be no doubt that they constitute the framework of the subject with which one is dealing; but it is possible to be overburdened with bibliographies, and for the general reader they are of minor importance so long as the facts have been extracted out of them and are presented to him in attractive form and with reasonable fulness. I shall, therefore, generally place them at the end of the descriptions; the individual references will be arranged neither alphabetically nor chronologically, but simply in the order in which they are alluded to in the text. The serious student, who may wish to investigate fully any special type, will find useful literature lists in Taruffi's compendious work (*Storia della teratologia*) and in the *Index Catalogue* of the Washington Library.

The types selected for description in this chapter are not, so to say, typical types; they have been chosen because they are not typical. Let it be borne in mind that the pathology of the embryo deals with malformations, with disturbances of ontogenesis and organogenesis; in this respect it differs from the pathology of the fœtus, which has to do with diseases, with disturbances in the performance of the functions of formed organs. It follows, therefore, that the types of embryonic pathology are monstrosities, while those of fœtal pathology are antenatal diseases. Now, the types which are to be described in the following pages are neither malformations nor diseases, although they are doubtless related to both: they are disturbances of growth, and growth is a phenomenon common to embryonic and to fœtal life. Indeed, growth is common to the early part of postnatal existence as well as to the whole of antenatal life. Disturbances of growth, therefore, are not typical of embryonic pathology; they are not even typical of antenatal as contrasted with postnatal pathology. Dwarfism, giantism, and hemi-hypertrophy are, in consequence, quite non-typical of embryonic pathology; but they are of great value on this account, for they serve as connecting links between the pathology of the fœtus and that of the embryo, and even between the pathology of the child and that of the unborn infant. They are placed here because they bridge over the gap between Section I. of this Manual and the present part; they give the reader a general idea of the resemblances which exist between the pathological processes of the antenatal and postnatal parts of life. He will very soon be dealing with the dissimilarities, and it will be necessary for him to remember that there are some similarities after all, although they may be few in number. So, because they are not typical of embryonic pathology, the anomalies of growth are taken here and made to serve as an introduction to the types which are in every sense typical of embryonic pathology.

Microsomia (Dwarfism).

Microsomia is a better name than dwarfism for the teratological type to be described. The word "dwarf" is very old, and in its progress down the centuries it has gradually taken on various meanings, and in none of these is it exactly synonymous with microsomia. To most people, "dwarf" means a diminutive adult human being, bringing with it memories of General Tom Thumb, the Midgets, and one of Sir Walter Scott's characters. To a few persons, well read in Spenser's *Faerie Queene* and mediæval romances, it signifies an attendant upon a knight or a lady; and to some others, versed in mythological lore, it suggests the race of metal-working and (too often also) mischief-working elves. Even in its restricted meaning of a diminutive adult, it includes cases of stunted stature due to postnatal diseases of the spine and of the lower limbs; and it has been applied to the results of antenatal maladies, such as achondroplasia. Microsomia is at once something less and something more than all these. It is more nearly equivalent to what Sir George Humphry (1) has called "true dwarfism," although it differs slightly even from that: a true dwarf is a person of unusually small stature, not as the result of any particular disease or deformity, but merely from growth having fallen much short of the usual standard. Microsomia I define as a "monstrous smallness" of all the parts of the individual, whether that individual be an embryo, a fœtus, a child, or an adult; for the age reached, the size is much below the normal, growth having been arrested. This definition introduces the possibility of the smallness being corrected or undone in a later period of existence, a modification which I regard as of some importance in relation to antenatal microsomia.

The following facts about growth in antenatal and in postnatal life are worth remembering in connection with microsomia. Growth is going on during the whole of antenatal life, with great rapidity in the early part of it, less quickly towards the close; but it does not cease at birth as everyone knows, for the infant continues to increase in size until he is a child, and the child goes on growing till the eighteenth or nineteenth year. It may be concluded, therefore, that growth may be arrested either before or after birth, at any age between minus nine months and plus nineteen years. Consequently, microsomia may be antenatal or postnatal. It follows, further, that it may be arrested either in embryonic or in fœtal antenatal life, and that, therefore, there may be embryonic and fœtal microsomia. Facts in support of these statements will be brought forward immediately; in the meantime, let them be taken on trust, in order that I may lead the reader on to some other conclusions. Growth is not the only process going on at these different epochs of life. In embryonic existence growth is accompanied by, nay, is overshadowed by development or ontogenesis; increase in size is made almost insignificant by increase in complexity; accrescence is hidden by organogenesis. Growth asserts itself in fœtal life, for the processes of ontogenesis have slackened; but there is still some development going on, and so the two vital phenomena run on side by side. But further, in fœtal life the formed organs have begun to perform functions, and so a third manifestation of life is added to the other two. There is growth and development and the performance of organic functions; possibly the order of arrangement represents the order of their importance at this period of antenatal life. After birth, both growth and development slacken very perceptibly, indeed ontogenesis almost disappears and is represented only by some changes in the brain and genital organs, and by the process of dentition. On the other hand, the physiological activities of the various organs greatly increase, and gradually a fourth series of vital processes, the mental, are superadded. Now the question arises—and it is an important one—when microsomia comes on at any of the periods above mentioned, will it be accompanied by an arrest of the other vital processes (ontogenesis, physiological activities of body and mind) which are peculiar to that period, or will it not? There is reason to believe that the arrest sometimes affects growth alone, and sometimes includes also the other activities of the individual. In the former case it must be assumed that the cause of the arrest, whatever it may be, has a discriminating power which enables it to pick out and stop the phenomena of growth alone; in the latter case it may be supposed that its action is a more general one, such as produces instances of dwarfism combined with malformations or with diseases or with mental obtuseness. There is also some evidence that one form of vital activity may be arrested while another is accelerated, although this would appear to be rare. Let us now turn to the recorded facts, and see how they accord with the statements which have just been made. Let us consider, in order, microsomia as it affects the embryo, the fœtus, and the child.

Embryonic Microsomia.

Sometimes when we are engaged in examining an abortion sac we find to our surprise that it contains an embryo of a size much smaller than the size of the sac had led us to expect. For instance, an abortion sac the size of a hen's egg may disclose an embryo only 2 or 4 mm. in length. This is what I understand by embryonic microsomia, and the embryo I call a "dwarf embryo." I have examined several specimens of this kind. One (2) was from the ninth pregnancy of a woman, thirty-six years of age, who had on two previous occasions miscarried. Three months after the cessation of menstruation she expelled an intact abortion sac measuring 7 cms. in length and 13 cms. in its minor circumference. It had the shape and size of a large hen's egg, and there was a small hæmorrhage in the decidual membranes near the narrow end of the ovoid. I ex-

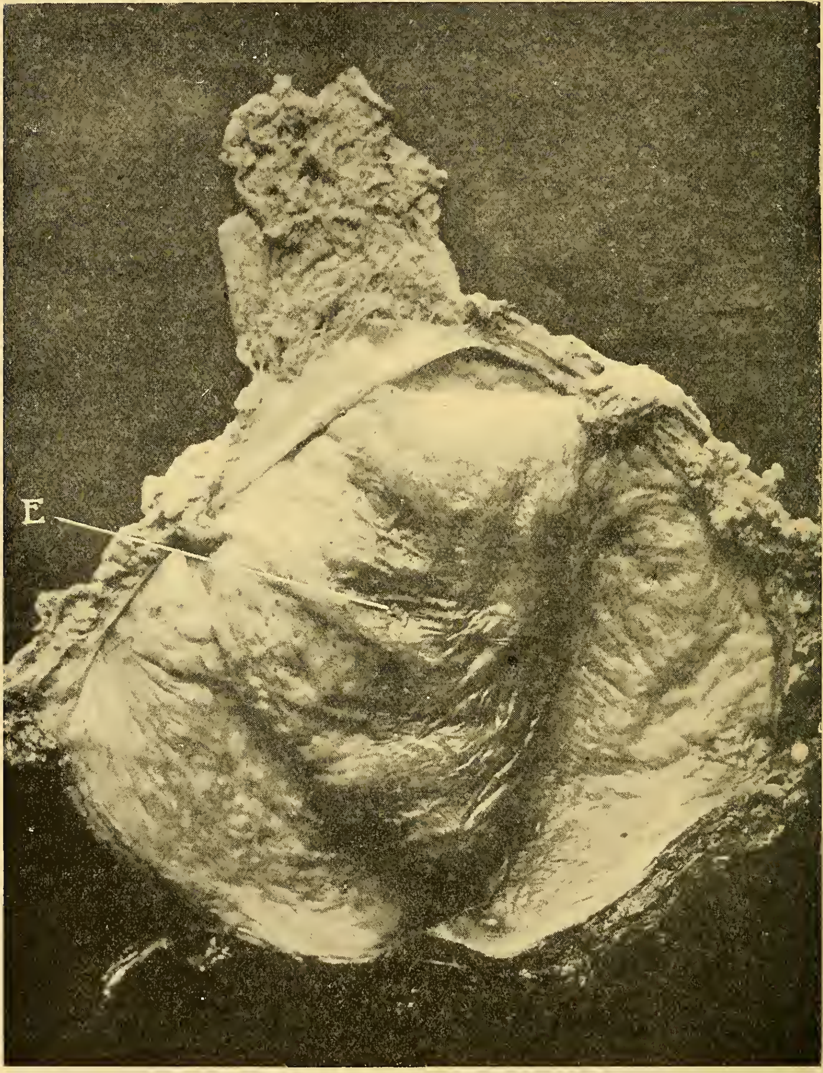

FIG. 38.—Abortion Sac, 13 cms. in circumference, containing dwarf embryo (E), 2 mm. in length. Specimen No. 42.

pected to find in it an embryo of about the length of 6 cms.; but the contents consisted of nothing more than a tablespoonful of somewhat muddy liquor amnii, and an embryo measuring little more than 2 mm. in length lying close to the sac-wall (Fig. 38). In another specimen (3), the sac measured 7 cms. by 5 cms., and contained 6 drms. of clear liquor amnii, and an embryo 4 mm. in length, with an umbilical vesicle (4·5 mm. in length) attached to it. In this case also there was a hæmorrhage in the decidual membranes, but at the broad end of the ovoid. The embryo showed no trace of limbs, while in the first case they were present but deformed. In yet another specimen which I have had an opportunity of examining (unpublished), the disproportion between the size of the embryo and the containing sac was not so great, but was still quite recognisable. In the second and third cases there had been two months amenorrhœa. Specimens not unlike the above have been described by other observers, as by Isbrand de Diemerbroeck (4), L. Ciniselli (5), and G. Colombo (6); but the most complete reports have come from His (7), C. Giacomini (8), and F. P. Mall (9).

I look upon these cases as instances of dwarfism of the embryo; but I need hardly add that they are not so regarded by all pathologists. According to some writers they are instances of early hydramnios: thus Keppie Paterson (10), not long ago, described a case of "hydramnios of the ovum," in which the amniotic sac was as large as at the third month of pregnancy, while the embryo was of the size of the third week. I had an opportunity of examining this specimen, and noted that the embryo had a development considerably in advance of its size; I, therefore, was inclined to regard it rather as a case of dwarfism of the embryo than of hydramnios. Doubtless there was an excess of liquor amnii, but the more important phenomenon was the embryonic microsomia. Other writers, again, have explained these abortion sacs as examples of early embryonic death with continued growth of the chorionic vesicle. I admit that it is quite possible that the chorion and decidual membranes may go on growing after embryonic death; for they have a large amount of individual vitality, so much that they have even been regarded as constituting a separate larval stage in human ontogenesis (J. Beard, 11). I do not, however, think that there is clear evidence of the death of the embryo in these cases; certainly in my specimens, which I examined by means of serial sections, there was no signs of anything more than recent death; the changes seen in them truly furnished me with a riddle in morbid ontogenesis which I have not yet succeeded in reading, but they did not appear to be of a post-mortem nature. At the same time, I freely admit that we know little about post-mortem changes in the embryo; thus, it is not, in my opinion, proven that the dead embryo can entirely disappear by dissolution in the liquor amnii. But, further, there is evidence of a positive kind in support of the view that these small embryos are instances of microsomia. Féré (12), in the course of his experimental work, almost constantly found dwarf chicks among the deformed ones; and Panum (*op. cit.*, 1860) and Dareste (*op. cit.*, 1891) also noted that teratogenic agencies produced an imperfect and unequal development of the area vasculosa with "atrophic" and dropsical embryos. Gerlach and Koch (13), by partially varnishing eggs in incubation, succeeded in getting partly dwarfed chicks, a result ascribed by them to diminished penetration of the shell by oxygen. Henry de Varigny's experiments (14) on the artificial production of dwarfism in fresh water snails (*Lymnæus stagnalis et auricularis*) have been quoted by some writers in connection with human microsomia, but the conditions of life are too dissimilar to permit of the drawing of any deductions therefrom; the same objection applies to the experiments of Driesch, Wilson, Zoja, Morgan, O. Schultze, and O. Hertwig (15), who worked with the eggs of sea urchins, medusæ, ctenophores, frogs, and of amphioxus, and who were able by destroying half the ovum (*e.g.* one blastomere in the two-blastomere stage) to get not half an embryo (as some other observers got) but an embryo half as large as usual.

There is, it seems to me, sufficient evidence, both clinical and experimental, to warrant a belief in the occurrence of microsomia or dwarfism of the embryo; but it does not, of course, follow that the causes of the arrested growth which have been demonstrated or suspected in the case of the chick will be found in action in the human subject. I am inclined to attach great importance to hæmorrhage into the decidual membranes as a determining cause of the dwarfism in the specimens seen by me; but other causes, predisposing and determining, may have a value. There are several other questions concerning embryonic microsomia to which no answer can as yet be given: thus, there is no information to be had as to the fate of a dwarf embryo when the pregnancy does not result in abortion. Does it become a dwarf fœtus? Is, on the other hand, the embryonic dwarfism replaced by accelerated growth in the fœtal period? We can say nothing with any definiteness, but analogy, as we shall see, suggests that the second hypothesis is the more likely one. There is another question which may be asked, and to which a sort of half answer may perhaps be given—Is embryonic microsomia commonly associated with embryonic malformations and monstrosities? As has been explained already, growth in embryonic life is concurrent with development (ontogenesis), and it is possible, therefore, that the cause that arrests growth and produces microsomia may also arrest ontogenesis and produce malformations. There is evidence that this sometimes happens: in one of my specimens the embryo was deformed as well as dwarfed, and one of Mall's cases showed club-hands and feet and a defective ear. There is also evidence that growth alone may be interfered with, the constructive processes going on normally. We do not know why it is that the arresting cause in some cases expends its force upon growth, and in other instances acts upon the constructive or architectonic part of embryonic existence; but apparently it is so. We shall see, further, that this character is not peculiar to embryonic microsomia. There is another question still that may be asked—May an accelerated rate of development in the embryo lead to a slackened rate of growth? The only hint of an answer that we can get to this question comes from Dareste's experimental work (16); he found that by over-heating eggs in incubation he was able to expedite development and to retard growth, and so get dwarf chicks.

In this, as in so many other parts of Antenatal Pathology, the *quæsita* are many and the *data* sadly few. The careful observer who wishes to make available new data will do well to examine carefully all abortion sacs.

Fœtal Microsomia.

Since fœtal life lasts for seven months it is theoretically possible that at any time in this period growth may be arrested and microsomia result; but, as a matter of fact, little is known of the earlier arrests, and we can only speak with certainty of the dwarfism which is recognised at birth at the full term. Obviously, a new-born infant may be small and yet not a dwarf; it may be prematurely born and small on that account. Of course it may be both dwarfed and prematurely born, but it will always be difficult to do more than suspect such a combination. The case easiest of recognition is that in which an infant is born at the full term of gestation (carefully calculated) with all the signs of maturity save size and weight; such an infant may be regarded as an instance of fœtal microsomia, it is a dwarf fœtus. If the dwarfism is accompanied by malformations, as there is reason to believe it often is, it becomes next to impossible to be certain regarding it, and the case will in all probability be classed by most observers as one of monstrosity and not as one of microsomia. To give some degree of definiteness to a somewhat indefinite subject, let us say that a fœtus born at the full term of pregnancy, weighing less than 3 lb. and measuring less than 12 inches in length, but possessing the other signs of maturity (finger-nails, absence of lanugo, etc.), is a case of fœtal microsomia.

Possible instances of microsomia occurring early in fœtal life are recorded by Montgomery (17), who described a fœtus of the size of two months in association with a placenta (diseased) of the size of three months, and by Cruveilhier (18), who discovered a fœtus of the size of two and a half months in a plural pregnancy of six months. In relation to Cruveilhier's case, it may be remarked that the presence of a co-twin in utero often has a dwarfing effect upon the other fœtus (in the human subject). Illustrative instances of full-time or nearly full-time fœtuses were these reported by Sir Everard Home (19), T. E. Baker (20), G. A. Mursick (21), and S. J. Scott (22). Of one of these we are fortunate in possessing the after-history; it deserves a paragraph to itself.

It is the case reported by Sir Everard Home some eighty years ago, and recently brought to light again by Hastings Gilford (23). The dwarf fœtus was the offspring of an Italian woman, who travelled with the Duke of Wellington's army, and who was so terrified by a monkey when three months pregnant that she was thrown into convulsions; she did not miscarry but went to the full time, and gave birth to a female child weighing 1 lb. and measuring 7 inches. This child grew up (to speak somewhat paradoxically), and was known as Caroline Crachami, "the Sicilian dwarf"; she was exhibited in London, and died at the age of nine years. She measured nearly 20 inches in height, and her ossification, dentition, and mental powers were those of a child of two rather than of nine years. In this case, therefore, there was both arrested growth and arrested development; and to the syndrome thus produced it has been proposed (23) to give the name "ateleiosis" (Gr. ἀτελής, unripe, imperfect), but it is doubtful whether any benefit flows from the introduction of the new term. Fœtal microsomia may or may not be accompanied by arrested development.

Several other well-known dwarfs seem to have been, in their origin, instances of fœtal microsomia. Nicholas Ferry, better known as Bébé (24), was born in 1741, when he weighed less than a pound, and had a length of 8 inches; at five years he weighed 9 lb. 7 oz., and was about 22 inches high; and he died when twenty-two years old (height then being 33 inches). He lived in the times when dwarfs formed part of the fashionable equipment of European Courts, and Bébé was devoted in a somewhat doglike way to his master Stanislaus, ex-King of Poland. He was apparently almost microcephalic, if we may judge from the details which Saint-Hilaire (24) gave about him. Another congenital dwarf was Antonio Toselli, who was described by L. Trevisani (25); he was born in 1808, and his mother, whose eighth child he was and was forty-six years of age at the time of his birth, had had an accident in the early months of her pregnancy. Antonio was very small at birth (full-time), and when twenty years old was only 40 inches in height. He had rather a large head. The "Princess Paulina" (26) was only 12 inches in length when born; at her death, aged nineteen, she measured 24 inches. The "Marquis Wolga" (27), born in Hungary in 1857, measured 9 inches at birth and weighed not quite 2 lb.; he married the liliputian "Marquise Louise." "Mary," known as the "Living Doll," was born in Hull in 1895, when she weighed not quite 1 lb. and measured 7 inches in length; at the age of four and a half years she was 17 inches high and weighed about 5 lb. (28). Other dwarfs who appear to have been dwarfs at birth were described by Dupuytren (29), Virey (30), P. Dubois (31), and by E. Magitot (32). Dupuytren's dwarf had the measurements of a five months' fœtus, although he was born at the full term; Virey's case, Babet Schreier or the "German Liliputian," was also the product of a full term pregnancy, although she only weighed 1½ lb. at birth and measured 6 inches in length; Dubois' dwarfess was the daughter of a dwarf father and a normal-sized mother, she had two dwarf sisters, and she herself gave birth to a premature fœtus weighing 3 lb. 12 oz.; and Magitot's dwarf, born in 1867, was very small when born, although his mother had arrived at the full term of pregnancy.

The causes of fœtal microsomia are as little known as those of embryonic dwarfism, and the reader will cease to wonder thereat if he will peruse what is written on p. 168 of the first section of this Manual on the subject of the variations in the normal weight of the fœtus. He will also be prepared, from his studies of teratogenesis (Chapters VIII. to XII.), to find the maternal impression alleged as a cause and maternal traumatism in pregnancy hinted at as a factor in the production of dwarfism. Doubtless the problem in its ultimate aspect is to be regarded as one of nutrition; doubtless, also, the state of the placenta has something to do with bringing nutritional defects into action; but beyond these general statements it is rash to go. The occasional occurrence of several dwarfs in one family, and the still more occasional occurrence of direct heredity in microsomia, make it evident that the arrestment of growth has been determined in the germinal period of life. Some further notes on etiology will be added after the description of postnatal microsomia.

Postnatal Microsomia.

All dwarfs are by no means born so; the retardation in growth may begin at one, two, three, or four years of age; indeed it may not commence until early adolescence. With these cases of postnatal dwarfism, antenatal pathology, properly speaking, has no concern, except in so far as they may be predisposed to by antenatal influences (heredity, postponed effect of fœtal and embryonic states); but a few paragraphs may be given to them, chiefly to show that the same laws apply to them as to embryonic and fœtal microsomia.

There is no evidence that Jeffery Hudson (33) was a congenital dwarf. He was born at Oakham, in Rutland, in 1619, and was scarcely 18 inches high at the age of nine years. His parents were of average height. He had some chequered experiences in a peculiarly adventurous life: he was presented "in a pie" to King Charles I.; he fought a successful duel, for "although a dwarf Jeffery was no dastard"; and he was sold as a slave in Barbary. This last and most trying adventure has a special interest for us, for it caused, or at least preceded, the recommencement of growth at the age of thirty years.

Joseph Boruwlaski (34) was born in Polish Galicia in 1739, and died in Durham in 1837 at the great age of ninety-eight. Shortness of stature, let it be noted, is not incompatible with length of days. He was never more than 39 inches in height. He had two brothers older than himself: one measured 41 inches and the other 6 feet 4 inches! Dwarfism may run in families, as we have said; true, but it sometimes runs alongside of giantism, as we now note. Boruwlaski also had a sister who measured only 2 feet 4 inches at her death, which took place when she was twenty years old. He was a great traveller, a good linguist, and wrote his own memoirs in an interesting fashion. He had several children of ordinary size.

Postnatal microsomia, then, is not always preceded by fœtal microsomia; nay, it sometimes develops in an individual who has been unusually large at birth. The famous "General Tom Thumb," for instance, was above the average weight of the new-born; the dwarf exhibited in London in 1848 (35) weighed 9 lb. at birth; John Thomson's dwarfed girl (36), whose thymus was found to be hypertrophied at the time of her death (age then four years and eight months), was a "big baby"; and F. Rohrer's case (37) was of at least normal dimensions when born. Further, postnatal microsomia may in some cases be temporary and give way to growth; thus, as has been already noted, the "strenuous" Jeffery Hudson began suddenly to increase in height at the age of thirty years, and, in more recent times, the dwarfess Magri (described by Taruffi, 38) grew after her nineteenth year. In this clinical fact lies the germ of the treatment of dwarfism, if it could be discovered what it is that retards growth.

Many causes have been alleged for postnatal dwarfism: among these may be mentioned poor or bad food, the infectious fevers, injuries (especially those affecting the head), chronic hydrocephalus, fœtal rickets (45), and idiocy. Of course several of these alleged causes might with equal probability be regarded as concomitant results of an as yet undiscovered etiological factor. Alcoholism of the parents has also been blamed: Langdon Down (39) found that three children begotten by a man during a period of excessive indulgence in alcohol were dwarfed, while those borne by his wife before and after the alcoholic period were normal. If we admit an antenatal cause in these cases of microsomia which do not develop till childhood, we must suppose that it remains latent or is held in check during the early months of life. The occasional occurrence of family prevalence in dwarfism would seem to make it necessary to admit not only an antenatal but even a germinal causal factor. This phenomenon of family prevalence was noted, it will be remembered, in the case of Boruwlaski; it was present also in the observation made by Clauder (40), in which each alternate child in a family of eight was a dwarf; less striking instances were those reported by C. Taruffi (41), Schaaffhausen (42), and G. O. Jacobsen (43). There was also direct heredity in P. Dubois' case (*loc. cit.*). Consanguinity and advanced age of the parents, if they could be substantiated as causes, would likewise favour the idea of a germinal etiological influence.

With postnatal, as with embryonic and fœtal microsomia, anomalies in development (malformations) may be found associated, but they are likely to be of a less grave type and they affect the structures developed in postnatal life alone. Thus, dentition may be incomplete or retarded; the general ossification of the skeleton may be tardy; the skin may be hairless and the fingers almost nailless (44); the reproductive organs may be defective, as shown by sterility and want of sexual instinct in both sexes, by cryptorchidy in the male, and by absence of pubic hair and delayed menstruation or oligomenorrhœa in the female; and the mental powers may be of a low order, pointing to incomplete development of the higher nerve centres. Of course, exceptions to all these statements can be discovered: some dwarfs, for instance, have been perfectly formed; some have been able to have children, generally of normal size; some have lived to a good age; and some have had fair intellectual powers. At the same time, I think it may be said that a general impression is left upon the mind that the dwarf is in many ways imperfectly fitted to fight the battle of life. Dwarfism and infantilism and idiocy have more than an occasional and accidental association (46).

Generalisations.

The reader will now realise that I was right when I described microsomia as a somewhat non-typical type, so to say, of embryonic pathology. Microsomia, as has been fully proved, may attack the organism in the fœtal and postnatal as well as in the embryonic period of life; it is not, consequently, peculiar to any one of these epochs. In each of them it may be accompanied by arrests of the other vital activities of the period, and these arrests show themselves in malformations and in the defective performance of such functions as those of reproduction and cerebration. It may also, apparently, be unaccompanied by these anomalies, growth alone being affected. There is some reason for thinking that the microsomia of one of these periods may be prolonged into the next; for instance, an embryonic dwarf may grow into a dwarf fœtus, and it, in its turn, may be continued into postnatal microsomia. There is also, however, some evidence to support the idea that sometimes the dwarfism of one period of life may be corrected in the next, and the dwarf fœtus, for instance, not become a dwarf child. There are also some fragments of proof that growth may recommence at an unusually advanced period of life.

Growth, by cell division, is the earliest vital phenomenon of the impregnated ovum; and it continues during the whole progress of antenatal life and stretches on into postnatal existence. There is growth, therefore, before there is an embryo and before there are any organs; growth also continues after all the organs and tissues have appeared. These facts are to be kept in mind when we try to arrive at any conclusions regarding the causes of the arrest of growth and of the dwarfism or microsomia that follows it. In the early stages of antenatal life the arrest obviously cannot be due to inaction or over-action of any separate organ, for separate organs do not then exist; at a later stage it may be so caused, but, if so, it becomes necessary to admit different causes for different periods of life. It is evident that there must either be a common cause of arrest which is in action during the whole of life, antenatal and postnatal; or there must be special causes for the special periods. I am inclined to think that the predisposing cause of microsomia is often in the impregnated ovum, and that in each of the succeeding periods of life certain circumstances may serve to prevent or to accelerate its action as the case may be. Syphilis, which is adduced as an important factor by Fournier (48), can hardly be the common cause for which we are looking.

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Macrosomia (Giantism).

Macrosomia is the converse of microsomia, and may be defined as a "monstrous largeness" of all the parts of the individual. It may, like microsomia, have its origin before or after birth, but the more characteristic cases are postnatal. It is, therefore, comparatively unimportant from the standpoint of antenatal pathology; and I shall give no lengthy description of it, but simply some condensed notes, some facts extracted from a scattered literature and compressed within limits.

Concerning *embryonic macrosomia* or giantism of the embryo, little or nothing is known. Theoretically, it may be expected to be met with, as much as embryonic microsomia; but there is next to no proof thereof. Mall's case (1) of an amniotic sac too small for its contained embryo may perhaps be regarded as one of an embryo too large for its containing amniotic sac. Experimental teratogeny, however, throws a little light here: Féré (2) found that substances which produce dwarfing or deformity of the chick embryo will sometimes cause excessive growth with or without excessive development (ontogenesis); and exaltation or depression of growth or development apparently depends upon the dose of the teratogenic agent and the "individual trophic equation of the germ." Of course, this "trophic equation of the germ," being, so to say, a personal equation, is not easily to be calculated. If it could be determined, many other problems than those of microsomia and macrosomia would be in a fair way to settlement. Embryonic macrosomia lies meanwhile in a neglected corner of Antenatal Pathology, which the systematic examination of early abortion sacs may yet serve to redeem.

Fœtal macrosomia or giantism of the fœtus, on the other hand, is well known. Of course, a new-born infant with a weight above the normal is not necessarily an instance of fœtal macrosomia; it may be simply a case of postmaturity, the child having by his longer sojourn in the uterus acquired an increased size and weight. Macrosomia is an undue largeness of the fœtus for the time in antenatal life arrived at. It must also be kept in mind, however, that a postmature infant may be at the same time the subject of macrosomia, as in Rachel and Neumer's case (3), and in Fuchs' two cases (49). The great criterion of macrosomia is weight, whereas postmaturity is characterised by advanced development (ontogenesis) as well. In the "problem of the postmature infant" (4), I have discussed this and allied questions, and I refer the reader, who is interested in the matter, to it. The postmature infant is larger and further developed than the ordinary new-born child, simply because he has had a month or six weeks longer life in the uterus; the subject of macrosomia is larger than he ought to be for the age at which he has arrived, and he may be developed in proportion to his weight or only in proportion to his age. The two conditions may, as I have already indicated, be combined; but in the paper to which I have referred (4), a still more remarkable association was pointed out. One of the postmature infants therein described was also the subject of anencephaly (*i.e.* arrested development of the cranial vault), and at the same time exhibited in other parts of the skeleton a degree of ossification not equal to but actually in excess of that which the postmature condition warranted: this remarkable case, therefore, was at one and the same time an instance of macrosomia, of postmaturity, and of arrested development. Let us, however, direct our attention to the uncomplicated cases at present.

Some instances of fœtal macrosomia may be cited: S. S. Smith's case, 22 lb. (5); G. Olano's, 22 lb. (6); C. W. Chubb's, 21 lb. (7); A. R. Rice's, 20 lb. 2 oz. (8); W. P. Johnston's, 20 lb. (9); R. L. Dickinson's, 20 lb. (10); J. Perrins', 19¾ lb. (11); T. P. Satterwhite's, 19 lb. (12); the cases of O. O. Burgess (13), E. Gordon (14), and A. Meadows (15), 18 lb. each; T. Wilmot's, 17¾ lb. (16); the cases of Kilham (17) and R. P. Myers (18), 17½ lb. each; H. Ludwig's case, 17 lb. (19); the cases of H. A. Cooper (20) and G. Read (21), 16½ lb. each; F. S. Jaquett's, 16 lb. (22); C. Waller's, 15 lb. 15 oz. (23); H.

Oppenheimer's, 15½ lb. (24); E. R. Lewis' case, 15 lb. 3 oz. (25); W. E. Kirby's, 14 lb. 15 oz. (26); the cases of D. J. F. Bennett (27), A. Brothers (28), and Cameron (29), 14 lb. each; Maygrier's, 13½ lb. (30); the cases of A. H. Cuartero (31), G. G. Detharding (32), and B. Wolff (33), 12 lb. each; W. Woodward's, 11 lb. 10 oz. (34); and E. A. Tucker's, 11 lb. 6 oz. (35). A greater weight than any of the above was attained by the infant reported by A. P. Beach (36), but the father of it was 7 feet 7 inches in height and the mother 7 feet 9 inches; it was the second child, and weighed 23¾ lb. and had a length of 30 inches; the first child born to these same parents weighed 18 lb. and was 24 inches in length.

Many of these giant fœtuses died at birth, and it is unfortunate that as a rule no information is forthcoming regarding their morbid anatomy; others survived, but rarely have we any record of their after-history. A few details I have gathered together and present to the reader herewith.

The case recorded by Cameron (29) was that of a female child weighing 14 lb. at birth; she weighed 69 lb. at twelve months, and had a height of 35¼ inches; at seventeen months the weight was 98 lb.; she was weaned at two years, when also she began to walk. Great size was here maintained up to two years (we have no further information); but it was not accompanied by any physiological precocity, on the contrary there was delay in walking and possibly in other functions as well. But there is some evidence that large size at birth occasionally precedes a precocious puberty. The large size may not be maintained, but there is a premature development of hair on various parts of the body, and an early awakening of sexual functions (Kussmaul, 37). Stocker's case (38) was a most remarkable one: the giant infant was one of twins, both female; and their mother had altogether eleven children, including triplets once and twins twice; the large twin showed some signs of a vaginal discharge at birth, and regularly menstruated at the age of three years; when eight years old, she had all the appearance of a girl of twelve, measuring 139 cms. in height and having well-developed genitals and mammæ. Moreau's giant boy (39) weighed 16 lb. at birth; he had a beard at seven years; at ten he measured 4 feet 5 inches; his testicles were large; and he was very powerful, but of a timid disposition. Apparently, the big boy of Willingham—"Prodigium Willinghamense," as Dawkes styled him (40)—was of large size from birth. He was born at Willingham, near Cambridge, in 1741; before he was three years old he was 3 feet 8 inches in height, and had the marks of puberty. I do not know whether the case of early puberty described by Molitor (41) was also one of fœtal macrosomia, as I have not been able to refer to the original article: it was that of a girl who had hair on the pubes at birth; puberty came on at four years; when eight years old she measured 133 cms. (53 inches) in height; soon thereafter she became pregnant, had intractable vomiting and jaundice, and expelled a hydatid mole containing a small embryo (35 mm. in length); she had large breasts and long hair. By a curious coincidence, the earliest pregnancy that I have met with also terminated in the expulsion of a hydatid mole: it was the case of a Polish Jewess, aged fifteen and a half years, who was said to have been impregnated by her cousin, a boy of thirteen years; she was large for her age.

From these case-records it will be clear that fœtal macrosomia may come into relation with several postnatally developed morbid states: it may, for instance, run on into infantile macrosomia ("pedomacrosomia," Taruffi); it may be followed by a precocious puberty, by early menstruation, and by an early pregnancy; and there is some evidence to show that it may be associated with the growth of tumours of the ovaries and testicles. J. Halliday Croom (42), for example, reported a case of ovarian sarcoma in a child of seven years who had many signs of precocious puberty, and about whom it was stated that her mammary glands were large even at birth. E. Sacchi (43), also, put on record an instance of infantile macrosomia in a boy, who, in addition to having an early puberty, was the subject of a tumour of the left testicle of an epithelial nature and containing coccidia; it is a noteworthy fact that the removal of the testicular tumour was followed not only by an arrestment of growth, but by the disappearance of some of the signs of sexual maturity. These various morbid states, however, lie outside the province of Antenatal Pathology; so also does true giantism ("neanio-macrosomia," Gr. νεανίας, young man, Taruffi) and the conditions which are related to it (acromegaly, leontiasis ossea, etc.), in which the excessive growth of the individual begins at or after the fourteenth year. They may, of course, be antenatal in origin although postnatal in development, and be the postponed effects of causes acting before birth; but so may many other morbid conditions, and it is necessary somewhere to draw the line bounding this ever growing province of Medicine.

The causes of macrosomia are even less understood than are those of microsomia. Speculation, however, has travelled along very much the same lines, but it would be of little profit to follow it. A few conclusions seem warranted, but even these must be accepted with caution, and will probably ere long call for revision. Great size at birth (fœtal macrosomia) and giantism developed later would seem to be commoner in the races in which the average height is great; great height is sometimes hereditarily transmitted, but in many cases there is no such transmission; macrosomia and sexual precocity are sometimes associated, but on the other hand the giantism of adolescence sometimes appears to follow as a consequence of premature cessation of sexual development (45); and, from what is known of the morbid anatomy of acromegaly and of its relations with giantism, it may be that increased growth is due to disease of some organ which normally checks growth, or to increased activity of some other organ which normally stimulates it. In relation to the last statement, it is interesting to remember that the large fœtus described by B. Wolff (33) had a disproportionately large heart and disproportionately small thymus and thyroid glands; interesting, but not, in all probability, throwing much light on etiology. If it turn out to be true that macrosomia is due to sexual infantilism and to retarded ossification of the epiphyses (46, 47), then, after all, this anomaly will have to be reckoned as an arrest.

In all speculations about the etiology of anomalies of growth, it has constantly to be borne in mind that a theory to be satisfactory must account for the facts, and for all the facts. Now, since both dwarfism and giantism may be antenatal as well as postnatal in origin, a theory of causation to be acceptable must be capable of application to the conditions which prevail both before and after birth; it must also take into account and explain the commonly associated conditions, such as infantilism in microsomia and precocious puberty in macrosomia (or *vice versâ*) and malformations in both; and it must also give a reason why these commonly associated states are not constantly associated. I know of no theory which fulfils these requirements; certainly, the idea of variations in the "trophic equation of the germ" brings us no nearer the truth than to say that a person with a high temperature is suffering from a thermometric perturbation. Syphilis, likewise, does not explain all the circumstances.

Therapia nulla.—It may yet be found that one of the organic extracts may check excessive growth, and so an empiric mode of treatment be rendered possible; but of that there is no indication now.

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Unilateral Macrosomia (Hemi-hypertrophy).

Unilateral Macrosomia, more commonly but less correctly termed Hemi-hypertrophy, may be considered here, although, strictly speaking, it is not a malformation of the whole body but only of one side of it. It is a one-sided enlargement of the individual, a "laterality" or asymmetry of the body. It has been supposed by J. B. Milne (1) and others that while the one side-half of the body is enlarged the other side-half is not normal but diminished or "atrophied"; if this be so, which is doubtful, then the malformation after all would be one affecting the whole individual.

A well-marked case of unilateral macrosomia draws attention by its strange and peculiar appearance. Proudly conscious, perhaps, of the strict symmetry of the two side-halves of his own body, the observer cannot but remark upon the grotesqueness of this anomaly or inequality of growth. But let him pause and inquire whether, after all, he himself is the possessor of perfect bilateral symmetry. Most probably he will find that he is not—his boots, gloves, and photographs bearing witness against him; more than this, he will most likely discover that he is unequally asymmetrical, while the subject of unilateral macrosomia may be, so to say, equally asymmetrical. It is the irregularity of his asymmetry that makes him normal, while it is the regularity of the asymmetry of the individual with hemi-hypertrophy that makes *him* abnormal. A strange paradox surely!

It would indeed appear to be true that the two side-halves of the body have a symmetry which is never entirely perfect. "Invariably Nature varies" (Paget, 2); and the two halves of the head and face, the two eyes and ears, the two arms and legs, and even the two breasts are slightly unlike in everyone. The right arm is usually longer and thicker than the left (Tuckerman, 3); the right leg may also have dimensions which exceed those of the left, but some statistics (*e.g.* those of G. Guldberg, 4) have shown the left leg larger than the right. Crossed asymmetry has been noted—right arm larger than left, but left leg larger than right—in 40 per cent. according to Guldberg; along with this morphological inequality it has been discovered that there is often a functional asymmetry (one side stronger than the other), and in this association has been found a possible explanation of why it is that a person lost in a fog tends to wander in a circle.

Unilateral macrosomia, however, differs from this "normal" or "physiological" inequality. In it the laterality is complete, or nearly so: all the parts on one side of the body are enlarged; they are usually enlarged in all their constituent parts; and in general they are proportionately enlarged. These, at any rate, were the characters of the case of unilateral macrosomia which I had an opportunity of examining with Dr. J. S. Fowler in March 1899. The details of this example of unilateral macrosomia were afterwards published by Fowler and Johnston (5), and are accessible to the reader; for this reason I shall be brief in my references thereto.

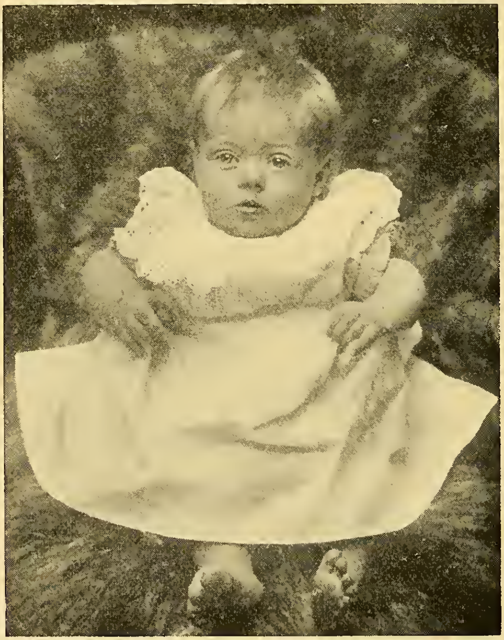

Fig. 39.—Case of Hemi-Hypertrophy or Unilateral Macrosomia. No. 224.

The patient, a little girl, was ten months old when I saw her; was the first child of healthy parents (ages twenty-two and nineteen) with no hereditary history of malformations; had been artificially fed, but had had no serious illnesses. The right foot had been observed to be larger than the left at the time of birth, when, also, numerous capillary nævi had been noticed on various parts of the body. Only on the forehead were the nævi unilateral in their arrangement. With regard to size, the patient showed an almost complete laterality: the right side-half was larger than the left. The enlargement, it is true, was slightly more obvious in some parts than in others; thus, it was more noticeable in the forearm than in the upper arm, in the foot than in the leg, in the leg than in the thigh, and was hardly discernible in the nose and mouth, although quite perceptible in the ear and in the external genitals. The sensory functions were unimpaired, and the reflexes were not abnormal; but no reliable observations on the temperature of the two halves of the body could be made. The appearances are well displayed in Fig. 39.

Some additional facts regarding this striking malformation may be brought together here from various sources in order to give completeness to the clinical picture. As the individual grows in size the disproportion between the two sides of the body becomes more apparent, but there is no evidence that the larger side gains much, if at all, upon the smaller side; it would appear as if the one side-half had got, as it were, the start of the other, but does not further increase its lead. During dentition, it may be noticed that the teeth are cut sooner on the enlarged side than on the other (1); walking may be interfered with by the laterality of the body which causes some obliquity of the pelvis. The hair may grow more quickly on the enlarged side, may curl more, and be coarser in texture; there may be increased desquamation of epidermis, the nails may be thicker and curved, and there may be unilateral hyperhidrosis. The tongue and tonsils may also show laterality (Finlayson, 6); or there may be macroglossia of the whole tongue (Kopal, 7), due to the enlargement of its muscle. One testicle may be larger than the other (Redard, 8). The internal organs have been found to show unilateral hypertrophy as well as the external parts; thus, at the autopsy in Arnheim's case, even the valves of the right side of the heart were larger than those of the left (9). Other malformations may be present, but rarely; for example, there was polydactyly in the cases of Bull (10) and Reuscher (11), and syndactyly in that of Wittelshöfer (12). Fœtal macrosomia may coexist (Hymanson, 13).

The general health is usually uninterfered with, but occasionally the mental powers may be weak (J. Thomson, 14). The enlarged parts would appear to be more liable to ulceration, to erysipelatous infection, and to lymphangitis. The association of nævi and telangiectases with lateral macrosomia has been noted in several cases, *e.g.* S. S. Adams' (15) and R. Duzéa's (16); but it is most noteworthy that these vascular disturbances have seldom been strictly unilateral in their distribution, a fact which militates against the theory advanced by Trélat and Monod (17) and Duzéa (16) that they are the cause of the macrosomia.

Knowledge regarding the etiology and teratogenesis of unilateral macrosomia is sadly lacking; theories there are in plenty and of the greatest variety, but no uniformity of belief. In Demme's case of congenital hemi-hypertrophy of the muscles in a female infant (30), it was thought (after the autopsy) that there was an increased number of ganglion cells in the anterior horns on the left side in the cord and in the nucleus of the hypoglossal (the tongue showed remarkable hemi-hypertrophy); and Demme thought the malady showed analogies with Thomsen's disease on the one hand and with pseudo-hypertrophic paralysis on the other. It is difficult, however, to formulate a theory of origin from these data and resemblances. Syphilis, maternal impressions, heredity, and injuries have been adduced, and have been supposed to act through disturbances of the vessels, lymphatics, or nerves of the affected parts; further, all sorts of ingenious explanations have been brought forward to account for the morbid anatomy of the malformation, but no satisfactory reason has yet been alleged for its one-sided character. It is no explanation to point out that some other antenatal morbid states, such as nævus neuroticus unius lateris, congenital white streaks (28), and tumours (29), have this unilateral character; this brings us no nearer the cause. It would be a real help if it could be shown whether the macrosomia develops in the fœtal period or is already present in the embryonic. There is, as the reader will remember, a degree of spirality about the embryo at the third week, but I know not whether along with it there may be also a predominance of one side of the body over the other. In some measurements made upon embryos and fœtuses by L. W. Fox (27) it was found that in the region of the face the right side was larger than the left; but the observations were too few (seven) to warrant their use in deciding the question of embryonic laterality. If unilateral macrosomia can be shown to be present in embryonic life, then Leblanc's theory of the action of the metameres (18) may be accepted as giving the most probable explanation of its mode of origin; but it must be kept in mind that metamerism[1] itself is as yet but a theory, and not an established fact in ontogenesis. It may be asked whether the latericumbent position of the embryo in the embryonic area has any causal effect; but no answer can be given. The statement that congenital hemi-hypertrophy is due to "an inherent tendency of the tissues to appropriate an excess of nutriment" is more ingenuous than ingenious. We may frankly admit that we do not know the causes of unilateral macrosomia or their mode of action; indeed we do not know those of general macrosomia, and we can hardly, therefore, expect to be more successful in our attempts to arrive at these of the partial variety of giant growth. It may be noted, before the subject is left, that the enlargement, as a rule, affects all the layers of tissue of which the part is made up (skin, subcutaneous tissue, muscle, bone); it is not, therefore, to be confounded with congenital elephantiasis (*vide* MANUAL, i. 300).

Literature.—(1) J. B. MILNE, *Quart. Med. Journ.*, iii. 243, 1894–95; *Lancet*, i. for 1895, p. 752. (2) Sir JAS. PAGET, *Internat. Journ. Med. Sc.*, n.s., xci. 41, 1886. (3) F. TUCKERMAN, *Journ. Anat. and Physiol.*, xix. 307, 1885. (4) G. GULDBERG, *Norsk. Mag. f. Laegevidensk.*, 4 R., xii. 180, 1897. (5) J. S. FOWLER and R. J. JOHNSTON, *Edinb. Hosp. Rep.*, vi. 113, 1900. (6) J. FINLAYSON, *Glasgow Med. Journ.*, 4 s., xxii. 327, 1884. (7) KOPAL, *Prag. med. Wchnschr.*, xx. 161, 341, 1895. (8) P. REDARD, *Arch. gén. de méd.*, i. for 1890, p. 31. (9) G. ARNHEIM, *Berl. klin.*

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[1] A metamere is a pair of mesodermic somites; it is supposed that the body is made up of a series of metameres, but it is difficult to trace this metameric arrangement in all regions of the embryo.

Wchnschr., xxxiii. 46, 1896. (10) G. J. Bull, *Boston Med. and Surg. Journ.*, xciii. 293, 1875. (11) C. Reuscher, "Bericht über einen Fall von totaler halbseitiger Körperhypertrophie," *Diss. inaug.*, Giessen, 1897. (12) Wittelshöfer, *Arch. f. klin. Chir.*, xxiv. 57, 1879. (13) A. Hymanson, *Arch. Pediat.*, xx. 428, 1903. (14) J. Thomson, *Edinb. Med. Journ.*, xxxvii. 249, 1892. (15) S. S. Adams, *Arch. Pediat.*, xi. 901, 1894. (16) R. Duzéa, "Sur quelques troubles de développement du squelette dus à des angiomes superficiels," *Thèse*, Lyon, 1886. (17) U. Trélat et A. Monod, *Arch. gén. de méd.*, i. 536, 676, 1869. (18) E. Leblanc, *Thèse*, Paris, 1897. (19) A. Massonnaud, *Thèse*, Paris, 1874. (20) H. True et Masmejean, *Montpelier méd.*, 2 s., x. 257, 1888. (21) S. Hornstein, *Arch. f. path. Anat.*, cxxxiii. 440, 1893. (22) Duplay, *Gaz. hebd. d. méd.*, n.s., ii. 529, 1897. (23) C. Turbil, *Giorn. d. R. Accad. d. med. di Torino*, lix. 9, 1896. (24) R. Jasinski, *Przeglad lek.*, i. 83, 1893–94. (25) V. P. Zhukovski, *Arch. psichiat.*, xxvi. i. 1895. (26) P. Wagner, *Deutsche Ztschr. f. Chir.*, xxvi. 281, 1887. (27) L. W. Fox, *Mitth. a. d. embryol. Instit. d. k.-k. Univ. in Wien*, i. 280, 1880. (28) J. Hutchinson, *Smaller Atlas of Clinical Surgery*, Plates i. and ii., 1895. (29) *Ibid.*, Plate xliii. (30) Demme, *Wien. med. Blätt.*, xiv. 17, 1891.

Unilateral Microsomia.

In a certain sense every case of unilateral macrosomia might be regarded as one of unilateral microsomia; instead of looking upon the one side as hypertrophied or overgrown, we might look upon the other side as atrophied or undersized. The question of deciding which side is abnormal has usually been answered by finding which of the two sides departs further from the normal measurements of the body for the particular age arrived at. In this matter, especially in the case of the fœtus, it is of course quite possible to be in error, and it may be that among the cases of unilateral macrosomia have been included instances of unilateral microsomia. Further, it is also possible that just as the one side-half of the body exceeds the normal size, so the other side-half may not come up to it; the macrosomia of one side may be compensated, as it were, by a microsomia of the other side. In all these cases much depends upon the fixing of the normal size and measurements for the age of antenatal or postnatal life reached, and, unfortunately, little certainty has been attained to in this part of anthropometry.

The cases to which the name congenital unilateral microsomia may be given must not be those in which there is one-sided atrophy of the brain and cranium with atrophy of the opposite side of the body and limbs; such cases are to be accounted for in another way and come under another category (result of fœtal brain disease). Several of the reported instances of unilateral microsomia must be excluded on this account; and very few true cases are left. I have met with a malformed fœtus (exomphalos, facial fissures, tail-like projection, etc.) in which the right arm was manifestly stunted (Fig. 30); but it would be incorrect to call it an instance of unilateral microsomia, even if the right leg had also been small, so long as there was not right-sided smallness of the head. Scheiber's case (1), if not a genuine instance of unilateral atrophy or microsomia, is very nearly so: it was that of a boy with complete left-sided hemi-atrophy, who had had an attack of apoplexy at the age of seven years. The writer was uncertain as to the origin of the atrophy, and did not decide between a developmental fault and cerebral hæmorrhage; but he tentatively suggested that there might have been a developmental fault on one side of the brain and a hæmorrhage on the other side. N. Obolonsky's case (2), also, is not a clear instance of unilateral microsomia: it was a new-born male infant, with unilateral smallness of the left leg and left side of the body and of the middle fossa of the cranium on the left side; the left arm, however, showed no marked difference in size; there was also hydrocephalus, and there were pre-auricular appendages on both sides, malformations of the left hand (syndactyly and perodactyly), talipes varus of the left foot, a tail-like appendage, enlargement of the penis, and hypertrichosis in the lumbo-sacral region and on the left thigh; the two cerebral hemispheres were symmetrical. C. Hennig's case of hypertrichosis and hemi-atrophy (3) was one in which only the right arm showed evident smallness; Forster Brockman's instance of hemi-atrophy (4) was a dissecting-room body, about which no history was obtainable; and in Caizergues' patient (5) there had been fever with convulsions on one side at the age of two years. All these cases must therefore be excluded; but possibly that reported by Wallis Ord (6) may be looked upon as true unilateral microsomia: it was that of a girl of twelve years, whose whole right side below the level of the eyebrows was smaller than the left, who had no hemiplegia, and whose mother had had a severe fright during the time she was pregnant. Sumner Pixley's case of "congenital unilateral atrophy" (7) may likewise be a genuine instance.

It is quite evident, from what has been noted above, that very little is known about unilateral microsomia, that very few cases have been reported, and that no satisfactory explanation of their origin is forthcoming. It may be that some instances of unilateral macrosomia ought rightly to have been included here; it may also be suggested that both these morbid states (macrosomia and microsomia) take origin in the embryonic period by reason of some cause (*e.g.* pressure) which acts upon one side of the organism and not on the other; but facts are so scanty that hypotheses become more than usually dangerous. One thing, however, seems fairly certain: there is a form of congenital unilateral smallness of the body which is not satisfactorily to be accounted for by disease of the brain arising during fœtal life, and for which, therefore, it is necessary to look for an explanation in the embryonic or germinal period.

Literature.—(1) S. H. Scheiber, *Wien. klin. Wchnschr.*, v. 369, 1892. (2) N. Obolonsky, *Ztschr. f. Heilk.*, x. 246, 1890. (3) C. Hennig, *Jahrb. f. Kinderhlk.*, xl. 107, 1895. (4) F. Brockman, *Journ. Anat. and Physiol.*, x. 786, 1876. (5) Caizergues, *Montpel. méd.*, xliii. 151, 1879. (6) W. Ord, *Brit. Med. Journ.*, i. for 1895, p. 587. (7) S. Pixley, *Med. News*, xli. 146, 1883.

CHAPTER XV

Teratological Types : Merosomatous Terata : Partial Macrosomia affecting (1) the head and face, (2) the extremities, and (3) one extremity or part of an extremity ; Pathogenesis and Treatment : Partial Microsomia.

In the preceding chapter the pantosomatous terata, to use Taruffi's name for them, were dealt with. They were the malformations, it will be remembered, in which not a part but the whole of the organism was affected; the whole body, trunk as well as limbs, was enlarged (macrosomia) or diminished in size (microsomia). They were anomalies of growth rather than of organogenesis or construction, and on that account were not clearly typical of embryonic pathology; but it was noted that they were not uncommonly accompanied by errors of organogenesis, showing that the two kinds of anomaly may coexist, indeed tend to coexist. Unilateral macrosomia and microsomia were also considered, although in one sense they were not pantosomatous terata; but they were evidently closely allied to the generalised forms of giantism and dwarfism. Now, in the present chapter, I proceed to the description of the clearly localised monstrosities (*merosomatous terata* of Taruffi), selecting partial macrosomia as the first type. In this way the anomalies of growth, already considered, are seen to be linked on to the anomalies of construction, which are about to be discussed, by these intermediate types, unilateral and partial macrosomia.

Partial Macrosomia.

By partial or localised macrosomia is meant a local as contrasted with a general overgrowth of the body; one part, such as one-half of the face, a leg, an arm, or a toe, considerably exceeds the other parts in size; and the overgrowth, as a rule, involves all the constituent structures of the affected part. From the standpoint of Antenatal Pathology we have only to do with the congenital cases; and among them there are some which may be truly embryonic in origin while others are apparently fœtal. It is often exceedingly difficult to separate the giant growths which are really due to an original anomaly of growth from those which arise in the fœtal period of antenatal life and are caused by such diseases as congenital elephantiasis and angiomata; on this matter the reader will find some remarks in the first section of this Manual (pp. 300–305). Bearing these facts well in mind, we may proceed to consider macrosomia as it affects (1) one side of the face, (2) the arms or legs, or (3) one limb.

Partial Macrosomia of the Head and Face.—Lateral enlargement of the head and face would appear to be rather rare; but within recent years D. M. Greig (1) has succeeded in gathering together thirty-five illustrative cases, a great advance upon Taruffi's fourteen instances (2). In Greig's list, cases of congenital elephantiasis, of sarcoma, and of leontiasis ossea have been carefully weeded out. The bones and soft parts may both participate in the unilateral enlargement, or the soft parts alone, or the bones alone may be affected. When the latter alone are enlarged, the morbid state is commonly described as originating after birth, and this is quite in keeping with the general principles of the subject according to which early interference with the processes of growth have more widespread results. Statistics do not show marked predominance of one sex or of one side of the face in these cases, although some writers have thought that males suffer more than females, and that the right side is more often the site of the enlargement than the left (Barwell, 3).

The laterality of the head and face is usually unmistakable. The one cheek is larger than the other; the angle of the mouth of that side is lower; the alveolar portion of the superior maxilla, half the tongue, the ear, and the tonsil show hypertrophy (Ziehl, 4); so do the lips, the eyelids, half the nose (Schieck, 5), and even the teeth when they appear (Passauer, 6). There may be a more marked flow of saliva on the side which is enlarged. Sometimes, but not often, the lower jaw participates in the laterality (Schneider, 7). The subcutaneous tissue generally shows thickening, and there may be recognisable lipomata (Schneider, 7). The mental conditions may, as the infant grows, be discovered to be defective.

The causes which are usually alleged in connection with all teratological cases are also advanced to explain unilateral macrosomia of the head and face; and the theory that in some way the overgrowth is due to perverted action of the nervous system (fœtal meningitis) would appear to be the most probable. On the other hand, there is much to suggest that the macrosomia originates before the fœtal period of life, and therefore before fœtal diseases can be invoked as causative agencies. Our knowledge of the teratogenesis of this, as of all forms of macrosomia and microsomia, is, after all, close neighbour to nothing.

Literature.—(1) D. M. Greig, *Edinb. Hosp. Rep.*, v. 212, 1898. (2) C. Taruffi, *Storia della teratologia*, v. 410, 1889. (3) R. Barwell, *Med. Times and Gaz.*, i. for 1881, p. 361; *Trans. Path. Soc. Lond.*, xxxii. 282, 1880–81. (4) F. Ziehl, *Arch. f. path. Anat.*, xci. 92, 1883. (5) Schieck, *Berlin. klin. Wchnschr.*, xx. 700, 1883. (6) O. Passauer, *Arch. f. path. Anat.*, xxxvii. 410, 1866. (7) A. Schneider, *Diss. inaug.*, Strasburg, 1885. (8) N. Friedreich, *Arch. f. path. Anat.*, xxviii. 474, 1863. (9) E. Kiwull, *Fortschr. d. Med.*, viii. 121, 1890.

Macrosomia of the Extremities.—Sometimes all the four extremities exhibit a certain degree of enlargement; when this occurs in association with hypertrophy of the head the clinical picture formed is that of acromegaly. This malady occurs, as a rule, after adolescence, and so does not at all fall within the province of the antenatal pathologist. "Congenital" cases have been described (*e.g.* those of Cénas, 1, and Jacobson, 2); but it is doubtful whether the affection was true acromegaly. The tendency of the malady to be associated with giantism has been already noted; and it may itself be regarded as giantism occurring in adult life, and limited, therefore, to the parts of the body where growth is still possible—the terminal parts; it has been named, on this account, peripheral macrosomia (Taruffi). Its pathogenesis, like that of all the anomalies of growth, is quite uncertain; it may be due to the neoplasm of the pituitary body, so often found on post-mortem examination, but the evidence is by no means conclusive. It has also been regarded as a reversion to the type of the anthropoid ape, a theory which, if true (the writer very much doubts it), would bring the malady well within the province of the antenatal pathologist after all. Here we leave the matter, adding this one sentence that the cases in which the long bones participate in the overgrowth are probably to be regarded not as true acromegaly but as delayed giantism (*macrosomia serotina*, Taruffi).

A curious form of enlargement of the extremities has been described by H. Friedberg (3) and A. P. Gould (4); in it there is a sort of crossed macrosomia, the right leg and the left arm being hypertrophied (3), or the left leg, the left side of the head, and the right arm being the overgrown parts (4). In Friedberg's case there were also telangiectases and lipomata. Associated with this type of macrosomia is that in which both arms or both legs are affected (*bilateral macrosomia*, Taruffi). Gherini's patient (5) had both lower limbs enlarged, the left showing the macrosomatous state more than the right; there were also nævi on the skin; while in Boéchat's case (6) the enlargement affected the hands and had existed for four generations. E. Rapin (8) has reported a case of congenital œdema of the two upper limbs and of the right side of the face. Some years ago I received from Dr. P. H. Nightingale the photograph of a Siamese woman, which is reproduced here (Fig. 40); the whole of the left upper limb and the right hand are much enlarged, and the case appears to be one of bilateral macrosomia of a very marked type. I could get no details of her history beyond the facts that she lived, in 1895, at Klong Bang Luang, that she was forty-three years of age, and a widow. Both her hands measured 13 inches long and 7 inches broad; the forefinger was about 4 inches in diameter. She could use the ring and little fingers of the right hand for eating her rice, but the rest were useless. André Thomas (7) has reported a curious case of unilateral enlargement of the left arm and leg and of the right side of the face and tongue ("hemihypertrophie alterne").

Literature.—(1) Cénas, *Loire méd.*, ix. 313, 1890. (2) D. E. Jacobson, *Arch. f. path. Anat.*, cxxxix. 104, 1895. (3) H. Friedberg, *Arch. f. path. Anat.*, xl. 358, 1867. (4) A. P. Gould, *Trans. Path. Soc. Lond.*, xxxiii. 222, 1881–82. (5) A. Gherini, *Contribuzioni alla chirurgia sui bambini*,

3–6, 63–66, 1876. (6) Boéchat, *Congr. périod. internat. d. sc. méd.*, Genève, v. 691, 1878. (7) A. Thomas, *Nouv. iconogr. de la Salpêtrière*, xiv. 508, 1901. (8) E. Rapin, *Nouv. iconogr. de la Salpêtrière*, xiv. 493, 1901.

Macrosomia of one Extremity.—A considerable number of cases may be grouped together here, including those in which the whole of one limb or a part of it (an arm or leg, a foot or hand, or a digit) is the subject of congenital hypertrophy. According to Taruffi's statistics the upper extremity is more often affected than the lower, and the left side than the right. Such names as cheiromegaly, megalodactyly, pes gigas, macropodia, macrodactyly, and sciapody, have been given to these localised giant growths.

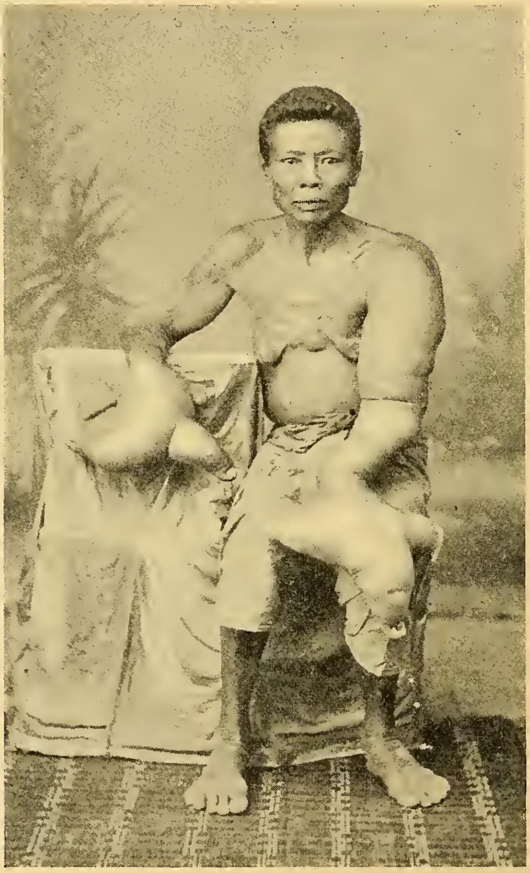


Fig. 40.—Siamese Woman with Bilateral Macrosomia affecting Upper Extremities.

In the cases in which the whole upper limb participated, it was occasionally found that there was some enlargement of the corresponding part of the chest (Wagner, 1). In several of the recorded instances, while the whole arm was larger than normal, only two or three of the fingers showed marked hypertrophy (Beck, 2; Höring, 3; MacGillivray, 4). Sometimes the macrosomia was limited to one hand; and the classical scholar will remember that the Persian king, Artaxerxes I., was named Longimanus or Macrochir because he was the subject of this localised form of giant growth. Less ancient instances have been reported by Guersant (5), F. Wulff (6), Ewald (7), D. Halderman (8), and Richardière (9). The commonest form of localised enlargement in the case of the upper limb is that which only involves one or two fingers (megalodactyly or macrodactyly). Fig. 41 represents a skiagram of this type of macrosomia; I am indebted for it to Dr G. Owen C. Mackness of Broughty Ferry. The patient in whom the deformity occurred was a boy, two years of age, and otherwise well formed; it was present at birth. In this instance the affected digits were the index and the thumb; but in the majority of cases the middle finger is the hypertrophied one (Annandale, 10; Curling, 11; and others). It is not uncommon for the enlarged digit to be dislocated or partially dislocated, and to lie more or less crosswise as regards the others. All the tissues of the part may be involved, and the metacarpal bone may likewise show enlargement (Rothschild et Brunier, 12). The fingers may be webbed (syndactyly) as well as enlarged (R. Abbe, 16; Bégouin et

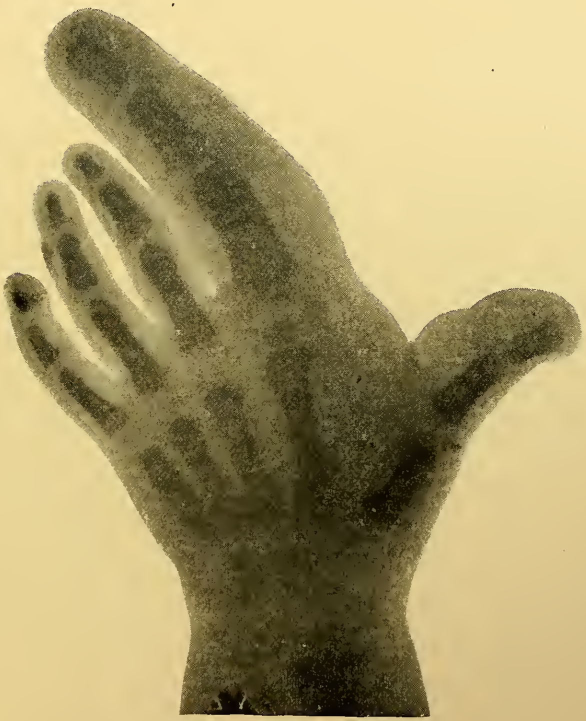


FIG. 41.—Case of Macrodactyly.

Sabrazès, 39), and there may also be a record of syndactyly in some relative of the patient (Morton, 13). In Cayla's case (14) there was asymmetry of the face and a certain degree of microcephaly; and Wahl's patient (15) was insane. The finger which is hypertrophied at birth may simply grow with the rest of the body; but it would seem that more often it increases at a disproportionately rapid rate, necessitating amputation (Lejars, 17). The examination of the amputated digit may show interphalangeal osteophytes and anchyloses (Planchu, 18); and as the head of the corresponding metacarpal may be similarly affected it is wise to remove it. Hypertrophy of a supernumerary digit (thumb) has been noted by Kirmisson (18*a*).

Sometimes it is the lower extremity that exhibits this partial form of macrosomia. The whole limb may be enlarged (Tesnières, 19); the enlargement may be associated with vascular nævi on the affected part (Adams, 20), or, somewhat curiously, on the limb of the opposite side (Chassaignac, 21); and there may be a great deposit of adipose tissue, which accounts in some measure for the great size of the extremity (Little, 22). The foot, again, may alone show hypertrophy, as in the cases reported by Busch (23), Albert (24), D'Urso (25), Platt (26), Blackader (27), and Allingham (28). In the instance described by Shoemaker (29), a brother of the patient had a supernumerary thumb; but most often, as in Galvani's case (30), there was no family history of deformities. Finally, to bring to a close this long list of partial macrosomias, the hypertrophy may affect only one or two of the toes. The great toe alone may be enlarged (Fuller, 31), or the second (Boehm, 32; Folier, 33), or the second and third (Pughe, 34), or the first and second (Taulier, 35), or the first and third (Fischer, 36), or the first, fourth, and fifth toes (*ibid.*). Not uncommonly, when two toes have been hypertrophied, these digits have been fused (syndactyly) as well; and in Carvallo's case (37) the syndactyly was present at birth but the hypertrophy only appeared at a later date. Hofmokl's observation (38) was peculiar: in it there was microdactyly at birth and afterwards hypertrophy of the second and third toes (macrodactyly) developed. In several other cases the enlarged digits continued to grow rapidly after birth, necessitating amputation. When the whole limb or a large part of it has been affected with macrosomia, ligature of the chief artery has occasionally been tried to check the growth, but with indecisive results.

Literature.—(1) Wagner, *Med. Jahrb. d. k. k. österr. Staates*, n.F., xix. 378, 1839. (2) Beck, *Med. Ann.*, Heidelberg, ii. 89, 1836. (3) Höring, *Med. Corr.-Bl. d. württemb. ärztl. Ver.*, xiv. 39, 1844. (4) P. H. MacGillivray, *Austral. Med. Journ.*, xvii. 9, 1872. (5) Guersant, *Bull. Soc. de chir. de Paris*, viii. 101, 1857–58. (6) F. Wulff, *St. Petersb. med. Ztschr.*, i. 281, 1861. (7) A. Ewald, *Arch. f. path. Anat.*, lvi. 421, 1872. (8) D. Halderman, *Med. Rec.*, xxiii. 320, 1883. (9) Richardière, *Bull. Soc. franç. de dermat. et syph.*, ii. 128, 1891. (10) T. Annandale, *Malformations . . . of the Fingers and Toes*, pp. 5, 6, 1866. (11) Curling, *Med. Chir. Trans.*, London, xxviii. 337, 1845. (12) H. de Rothschild et L. Brunier, *Rev. d'hyg. et de méd. infant.*, ii. 232, 1903. (13) T. K. Morton, *Med. News*, lxiv. 294, 1894. (14) Cayla, *Nouv.*

iconogr. de la Salpêtrière, xvi. 41, 1903. (15) L. Wahl, *Compt. rend. Soc. de biol.*, lv. 595, 1903. (16) R. Abbe, *Trans. New York Acad. Med.*, x. 639, 1894. (17) F. Lejars, *Nouv. iconogr. de la Salpêtrière*, xvi. 37, 1903. (18) Planchu, *Lyon méd.*, lxxxiv. 372, 1897. (18*a*) E. Kirmisson, *Traité des maladies chirurgicales d'origine congénitale*, p. 742, 1898. (19) Tesnières, *Rec. de. mém. de méd. . . . mil.*, xxix. 385, 1830. (20) J. Adams, *Lancet*, ii. for 1858, p. 140. (21) Chassaignac, *Bull. Soc. de chir. de Paris*, viii. 452, 1857–58. (22) Little, *Trans. Path. Soc. Lond.*, xvii. 434, 1865–66. (23) W. Busch, *Arch. f. klin. Chir.*, vii. 174, 1866. (24) E. Albert, *Wien. med. Presse*, xiii. 10, 71, 1872. (25) G. D'Urso, *Policlin.*, ii. 353, 1895. (26) Platt, *Bull. Johns Hopkins Hosp.*, vi. 49, 1895. (27) A. D. Blackader, *Arch. Pediat.*, i. 626, 1884. (28) H. W. Allingham, *Proc. Med. Soc. Lond.*, x. 106, 1886–87. (29) G. E. Shoemaker, *Med. News*, lxiv. 296, 1894. (30) Galvani, *Rev. d'orthop.*, ix. 421, 1898. (31) E. B. Fuller, *South African Med. Journ.*, vi. 13, 1898. (32) T. Boehm, *Diss. inaug.*, Giessen, 1856. (33) C. Folier, *Bull. d. sc. med. di Bologna*, 6 s., ix. 19, 1882. (34) R. M. Pughe, *Illust. Med. News*, v. 78, 1889. (35) Taulier, *Mem. et Compt. rend. Soc. d. sc. med. de Lyon*, (1867), vii. 75, 1868. (36) H. Fischer, *Deutsche Ztschr. f. Chir.*, xii. 57, 1879. (37) D. Carvallo, *El Progreso med.*, Chile, vi. 296, 1896. (38) Hofmokl, *Ber. d. k. k. Krankenanst. Rudolph-Stiftung in Wien*, p. 406, 1890. (39) P. Bégouin et J. Sabrazès, *Nouv. iconogr. de la Salpêtrière*, xiv. 305, 1901.

All these forms of partial macrosomia have a pathogenesis which is quite obscure. Doubtless they are due not to one but to several causes. Some of them are to be regarded as the result of fœtal diseases and are to be explained by lymphatic obstruction (Busey, 1) and lymphangiectasis, or by a diffuse fatty infiltration of the subcutaneous and muscular layers of the part (Duplouy, 2). I have seen a case of unilateral hypertrophy of the tongue in a young man shown by Mr. Wallace at the November Meeting of the Edinburgh Medico-Chirurgical Society (1903) in which lymphatic obstruction may possibly have been the cause of the enlargement. In other instances there is a general enlargement of all the structures in the part, and two theories have been invoked to explain them: the vascular theory of Trélat and Monod (3) and others which ascribes to slowing of the capillary circulation an increased nutritive activity of the tissues; and the nervous theory which looks to a trophic action of the special nerves of the part, and in order to explain the distribution of the hypertrophy has to have recourse to the idea of the hypothetical metameric arrangement of the body in embryonic life (Leblanc, 4). It seems to me that the cases of macrosomia in which all the tissues of the part are involved must be referred to causes acting before the fœtal period; but while accepting an embryonic cause, I do not think it necessary to regard it as nervous in its nature. I look upon the cause rather as a sort of tendency of the tissues to grow out of due proportion, a tendency present before the trophic action of the nervous system comes into play. I need hardly add, for the reader will already have it in his mind, that some of the cases of partial macrosomia can scarcely be separated from the neoplasms.

Three chief methods of treatment have been tried. First, elastic compression of the hypertrophied parts maintained for some time; second, ligature of the chief artery supplying the enlarged area; and, third, amputation of the digit, hand, foot, or entire limb. The first and second plans deserve a wider trial than they have yet received; the third, on the other hand, ought not to be so readily recommended and so hastily put into practice as has been done in the past, for it is sometimes followed by the excessive growth of neighbouring structures (*e.g.* other digits), and a hypertrophied part is sometimes more useful than none at all, while the æsthetic advantage is dubious. We may sum up in the words of Kirmisson (5): "le traitement . . . est loin jusqu'ici d'avoir donné des résultats brillants."

Literature.—(1) S. C. Busey, *Amer. Journ. Obst.*, x. 1, 223, 420, 571, 1877. (2) Duplouy, *Bull. et mém. Soc. de chir. de Paris*, n.s., xii. 343, 1886. (3) Trélat et Monod, *Arch. gén. de méd.*, i. 536, 676, 1869. (4) Leblanc, *Thèse*, Paris, 1897. (5) E. Kirmisson, *Traité des maladies chirurgicales*, p. 749, 1898.

Partial Microsomia (*Mero-microsomia*, Taruffi).

By *partial microsomia* is meant the disproportionate smallness of one part of the body as compared with the rest; it may be one side of the face or a limb or a digit. It is the converse, therefore, of partial macrosomia. It is as yet an ill-defined morbid entity; and time will be required before it is differentiated from localised atrophies coming on in infancy due to disease or defective development of the nervous system (*e.g.* poliomyelitis anterior) on the one hand, and from arrested growth of the limbs due to absence of one or more of the component bones (*e.g.* femur, radius, tibia) on the other. If these two groups of cases could be excluded we should then be left with the true instances of partial microsomia of antenatal origin. It has been thought that some of them may be caused by poliomyelitis anterior occurring in fœtal life, followed by paralytic club-foot and wasting of the limb, as in Wharton Sinkler's case (Keating's *Cyclopædia of Diseases of Children*, iv. 684, 1890), where there was also a maternal impression in pregnancy. Others, I think, are to be looked upon as intranatal in origin, and take their place in the group of obstetrical or birth palsies. But paralysis is by no means a constant accompaniment of microsomia. Yet others are due, there can be little doubt, to the pressure of amniotic bands or of the umbilical cord wound round a limb, as was described in Chapters X. and XI.; in such cases there may be no paralysis at all.

Further space, however, need not be given to the consideration of partial microsomia. As a matter of fact dwarfing in size of any part of the fœtus or embryo is usually accompanied by arrest in development; and since the latter is the more striking anomaly it absorbs attention, and the atrophic state which exists alongside of it passes almost unnoticed; the monstrosity or error in organogenesis overshadows the dwarfing, which is only an error in growth. A common instance of this combination of malformation with microsomia is found in syndactyly; here the fused or webbed fingers or toes are usually dwarfed in size. The reader will remember that syndactyly was also seen to be associated with macrosomia; but this is only another instance of the way in which both overgrowth and defective growth may be found along with the same type of malformation.

With reluctance we must leave this teratological type (partial microsomia) in its ill-defined state. Some earnest worker will one day, after much labour and great searching in the literature of the subject, be able to sort out from among a large number of cases of structural anomaly those in which true dwarfism of a part of the body exists independently of defective development of that part; but that day is, as yet, far off, and the type must perforce remain dim in our sight and obscure. Some of the difficulties, however, are even now capable of being removed and ought to be removed: for instance, a careful scrutiny of the cases ought to enable us to separate out those due to birth-injuries from those caused by fœtal disease of the nervous system, and those again from the cases in which morbid agencies have been at work in the embryonic epoch. Instances of microsomia of two or three toes and of a whole hand have been referred to by E. Fournier (*Stigmates dystrophiques de l'hérédo-syphilis*, p. 146, 1898), and might be used as the nucleus of a collection of cases of arrested growth apart from arrested development. Fournier ascribes them to the effect of the syphilitic poison, but does not in his description clearly distinguish between arrested growth and arrested development, a distinction which, I cannot help thinking, is of considerable importance.

CHAPTER XVI

Teratological Types: Merosomatous Terata (*cont.*): Monstrosities affecting the Spine and Head: Iniencephaly; Definition; Illustrative Instances; Morbid Anatomy and Clinical History; Associated Malformations; Teratogenesis; Literature.

The teratological types which now fall to be considered are those in which the spine is the region most involved. The reader will remember that it was decided (in Chapter XIII.) that it would be most convenient to adopt a regional classification of the monosomatous terata; and, in accordance with that decision, anomalies of the spinal column and its contents naturally take their place among the first types. After these have been discussed, I shall describe the monstrosities in which the head is the part most affected. There is, however, a very interesting type, known as iniencephaly, in which both the spine and the head are very constantly associated in malformation; it is convenient to deal with it first.

Iniencephaly.

In the monstrosity known as iniencephaly (Gr. ἰνίον, nape of the neck, and ἐγκέφαλος, the brain), the centre of interest is the nape of the neck or inion. Through the extreme backward bending of the head upon the dorsal region of the trunk the nape of the neck loses its external position and is enclosed within the somewhat globular mass which is formed by the head and the trunk (Plates XV., XVI., XVII., and Figs. 42–49). In well-marked specimens the nape of the neck may be described as the centre of this rounded head-body, from which the limbs stand out as little projections. The monstrosity well deserves the epithet of *très curieux* given to it by Isidore G. Saint-Hilaire (1), who was also the first to describe and to name it.

I have met with seven specimens of this type (Nos. 25, 44, 162, 225, 251, 252, and 277), a very exceptional experience if the great rarity spoken of by Saint-Hilaire be a correct representation of the facts (which I doubt). All these specimens showed very clearly the three cardinal characteristics of iniencephaly, to wit, imperfect formation of the occiput in the neighbourhood of the foramen magnum, spina bifida of considerable extent, and retroflexion or backward bending of the spine. The reader will best understand the monstrosity if I describe first a specimen showing a minor degree of it.

The fœtus whose external appearances are represented in Fig. 42 was given me for dissection by Dr. W. N. Elder in 1893, and was shown by me at a meeting of the Edinburgh Obstetrical Society in the same year (2). The noteworthy facts in the clinical history of the case were that the mother in her first pregnancy had given birth to a female child with a spina bifida, her second and third pregnancies had ended in the birth of normally formed male, and her fourth in that of the female iniencephalic fœtus to be described immediately. The labour was complicated by hydramnios. The mother was the younger of twins, and her mother had on two occasions given birth to twins; the father's mother had once had twins.

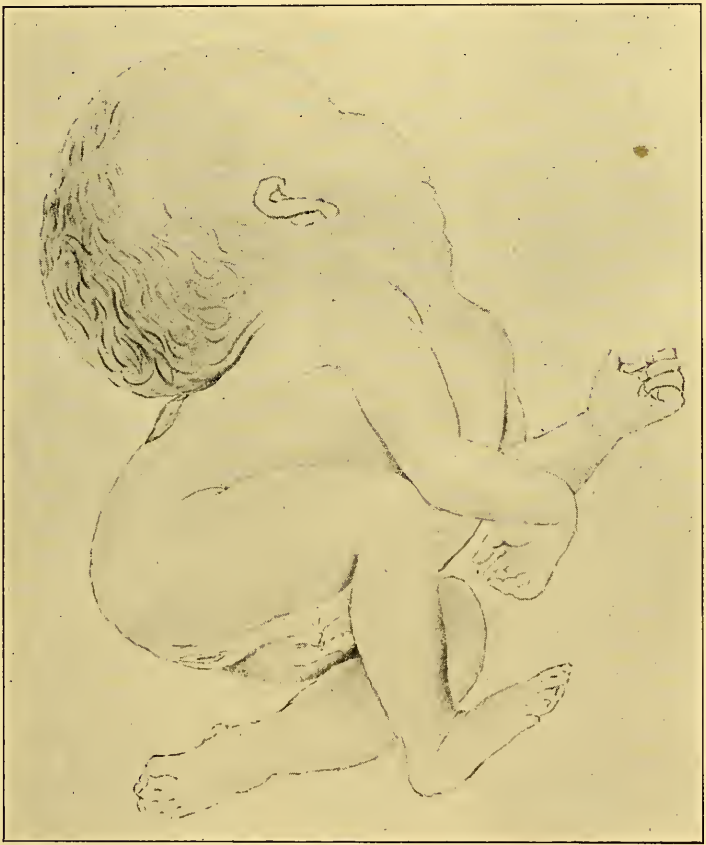


Fig. 42.—External Appearances of Female Iniencephalic Fœtus. Specimen No. 44.

The fœtus measured 30 cms. in length, and the mass formed by the head and trunk 19 cms. The face was directed upwards, and the whole head was sharply flexed backwards, so that the occiput came into close relation with the open spinal canal in the lumbar region. The skin of the head, however, was not continuous with that over the sacrum, and, in this respect, the specimen differed from the most marked type of iniencephaly. There was no indication of a neck-groove anteriorly, the skin passing directly from the chin to the thorax. The abdomen and thorax were prominent, but showed no defect. The vulva was normal, the anus was patent, and the limbs, although slender, were well formed.

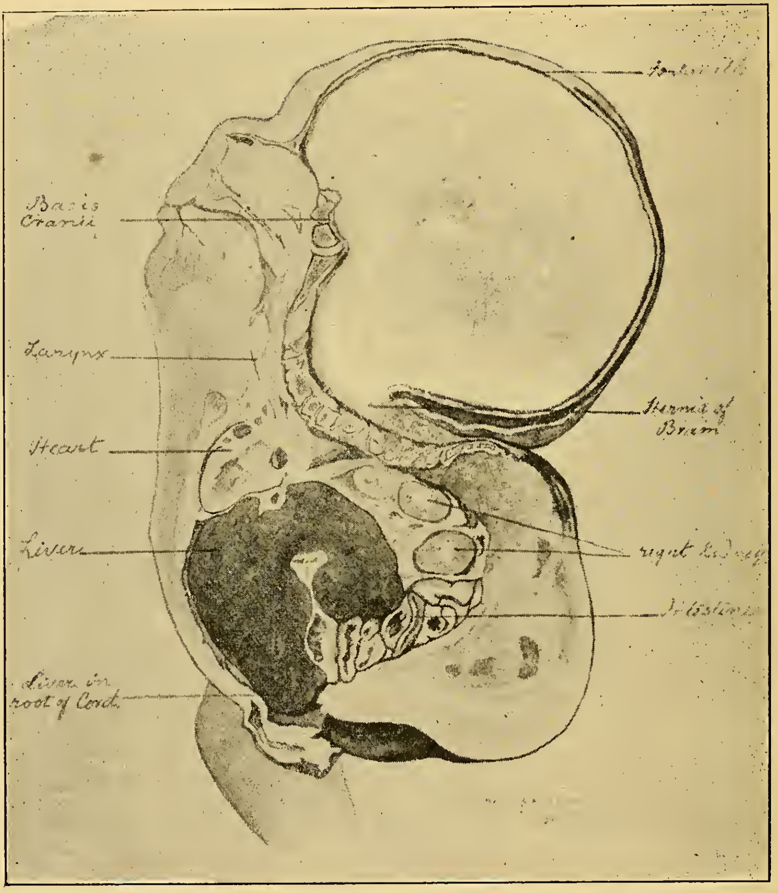
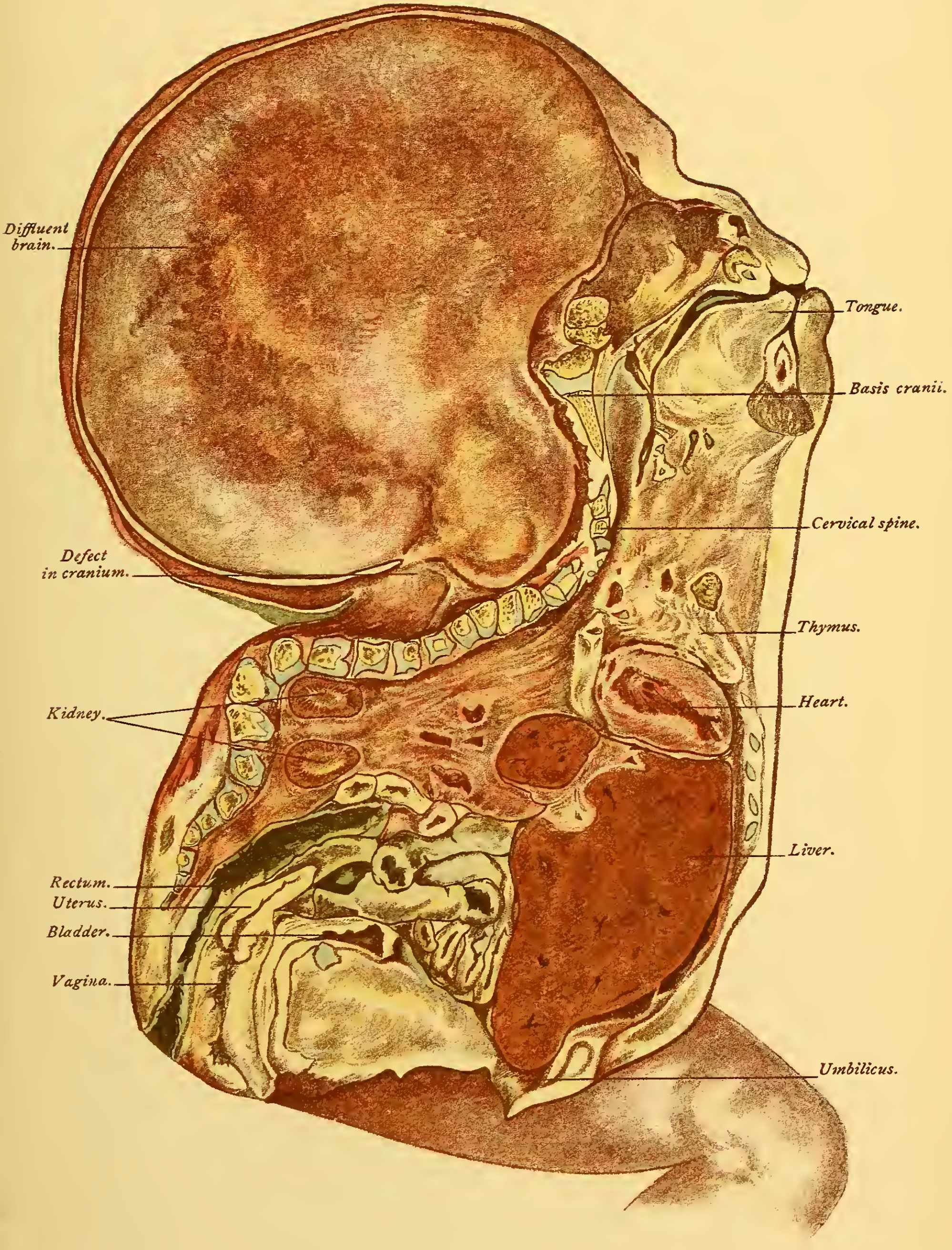


Fig. 43.—Internal Appearances of Iniencephalic Fœtus as seen in vertical mesial section. The parts are named in the Figure. Specimen No. 44.

The arrangement of parts in the interior of the fœtus was made plain by a vertical mesial section (Plate XV., Fig. 43); on account of slight lateral distortion of the trunk the middle line was not found in the whole of the section, the saw having passed a little to the

PLATE XV


Diffluent brain.
Tongue.
Basis cranii.
Cervical spine.
Defect in cranium.
Thymus.
Heart.
Kidney.
Liver.
Rectum.
Uterus.
Bladder.
Vagina.
Umbilicus.

right of it. From a study of the two surfaces of the section it is possible to understand the architecture of the monstrosity. Through the sharp backward flexion of the head it had come to pass that the spine passed upwards and forwards, and its cervical portion lay approximately at the centre of the mass formed by the fused head and trunk. The basis cranii looked directly backwards, while the anterior fontanelle, of fairly normal size, faced backwards as well as upwards. The bones of the cranium were thinner than normal; but, in addition, the occiput was in part wanting, and through the resulting aperture (an enlarged foramen magnum, we may call it) there was a protrusion of the brain substance. The brain, in fact, rested upon the exposed vertebral *bodies* in the cervical, dorsal, and lumbar regions, for there was a spina bifida in those portions of the column. On account of the retroflexion of the head, the herniated portion of the brain lay in a sort of artificial cavity. The skin of the head (as I have noted) was not continuous with that over the sacrum, and the lower part of the open spinal canal was visible in the lumbar region. The cerebro-spinal nervous system, therefore, was not entirely shut in as it is in the complete degree of iniencephaly. It is to be noted how the anterior margin of the liver projected into a small cavity at the root of the umbilical cord; in other specimens we shall see this cavity greatly enlarged, and a more marked protrusion of the abdominal contents taking place.

The fœtus, whose external and sectional appearances are shown in Figs. 44 and 45, was an example of the major degree of iniencephaly. I obtained it for examination from Professor A. R. Simpson, to whom it had been sent, without any clinical history, in 1888. I published the case in 1895 (3). It was a female, and in its external appearances it resembled a round mass with attached limbs; the round mass, as in the previous case, consisted of the head and trunk fused together in a very complete manner. The head was sharply flexed backwards, so that the skin covering its posterior surface was directly continuous with that covering the coccyx. There was no external sign of spina bifida; but the frozen section (Fig. 45) revealed the spinal canal open in its whole extent. The length of the fœtus was 26 cms., and that of the fused head and trunk was 13·5 cms.; the circumference of the head-trunk mass did not differ much at different levels. The distance from the occiput to the anus was only 5 cms. The face looked directly upwards, the nose was much flattened, the ears were deformed and sunk in deep grooves at the sides of the head, and there was no trace of a neck either anteriorly or posteriorly.

The internal appearances were made manifest by a vertical mesial (sagittal) frozen section (Fig. 45); in this, as in the former specimen, it was difficult to keep the middle line exactly, for the whole fœtus was somewhat twisted on its axis as well as retroflexed. In consequence of the twisting, the section in the pelvic region is to the left of the middle line, and the uterus, therefore, is not represented. It is evident at once that this specimen shows a more marked degree of iniencephaly than did the former one (Fig. 43).

The fœtal retroflexion is more nearly complete, the vertex of the head coming into close connection with the lower end of the spinal column; and the skin passes directly from the head to the gluteal region. The extraordinary distortion of the vertebral column is very evident; the cervical part lies nearly in the centre of the fœtal mass (fused head and trunk); from this point the column passes downwards and forwards at a short distance, and then turns backwards with a downward inclination to traverse the body and end near the skin surface immediately above the anus. There is no vertebral canal properly so called, for the spine is open in its whole extent; but, on account of the retroflexion, an artificial cavity, which may be called cephalo-rachidian, is formed. The cephalic and spinal parts of this cavity communicate freely through the defect in the squamous part of the occiput. The basis cranii is directed backwards, the oral aperture looks directly upwards, and there is no sign of a neck: these anomalies in construction are evidently associated with the sharp retroflexion of the whole fœtus. Further, through a defect in the postero-mesial part of the diaphragm, the spleen and intestines have been dislocated upwards into the thoracic cavity, where they lie behind the heart. Dissection revealed two small lungs, two kidneys and supra-renal capsules, and a normal uterus and annexa.

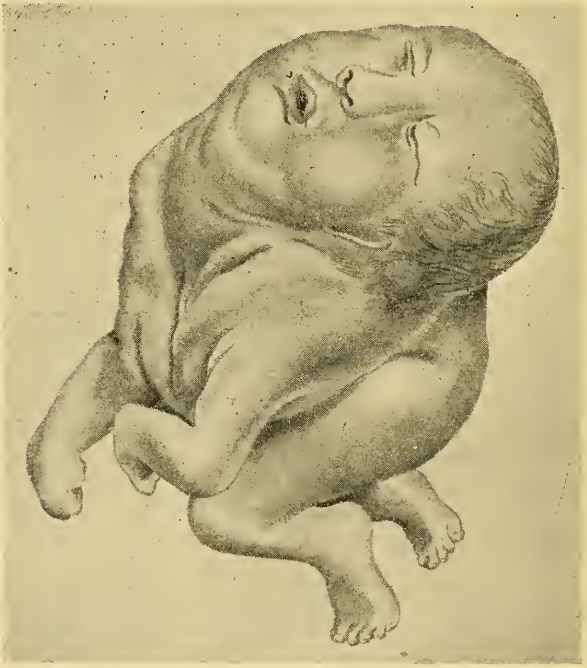


Fig. 44.—External Appearances of Female Iniencephalic Fœtus. Specimen No. 25.

In a small fœtus, which I received in April 1902 from Grimsby, the external appearances of iniencephaly are again very clearly shown (Fig. 46); unfortunately no clinical details came with the specimen. Another small iniencephalic fœtus (Fig. 47), a female, was sent to me by Dr. G. H. Pirie of Dundee in 1895 (4). It was the product of the tenth pregnancy of a woman, forty-two years of age, who had had eight full-time confinements and one previous miscarriage. The age of the pregnancy was between the sixth and seventh month, when the whole contents of the uterus came away intact. On opening the amniotic sac it was found that there was about a pint of thick liquor amnii of a yellow colour, and in it was

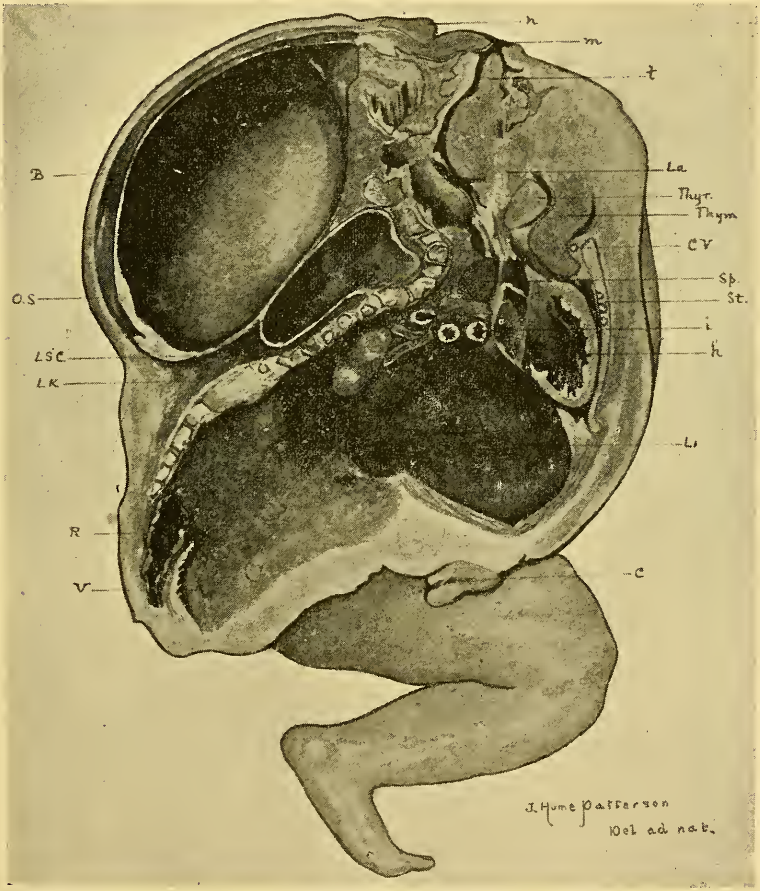


Fig. 45.—Internal Appearances of Iniencephalic Fœtus, as seen in a sagittal mesial section. *B.*, brain ; *C.*, umbilical cord ; *C.V.*, cervical vertebræ ; *h.*, heart ; *i.*, intestine ; *La.*, larynx ; *Li.*, liver ; *L.K.*, left kidney ; *L.S.C.*, left supra-renal capsule ; *m.*, mouth ; *n.*, nose ; *O.S.*, occipito-spinal space ; *R.*, rectum ; *Sp.*, spleen ; *St.*, sternum ; *t.*, tongue ; *Thyr.*, thyroid gland ; *Thym.*, thymus gland; *V.*, vagina.

the small iniencephalic fœtus attached by a cord 18 inches long. The fœtus was macerated, and had apparently been dead for over a month. When lying upon a plate, the monstrosity had sufficient resemblance to a frog to justify the comparison (Fig. 47). Yet another iniencephalic fœtus came into my hands in May 1900; it occurred in the practice of Dr. Murray Cairns of Liverpool, and was the cause of a prolonged labour.

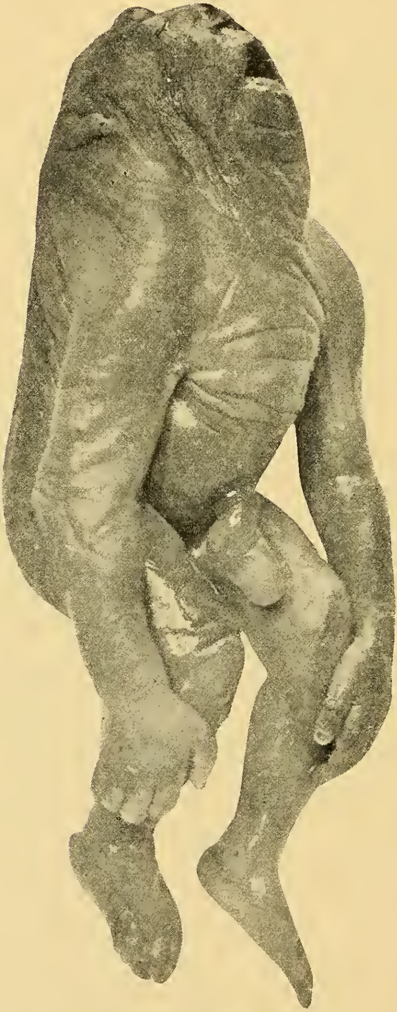
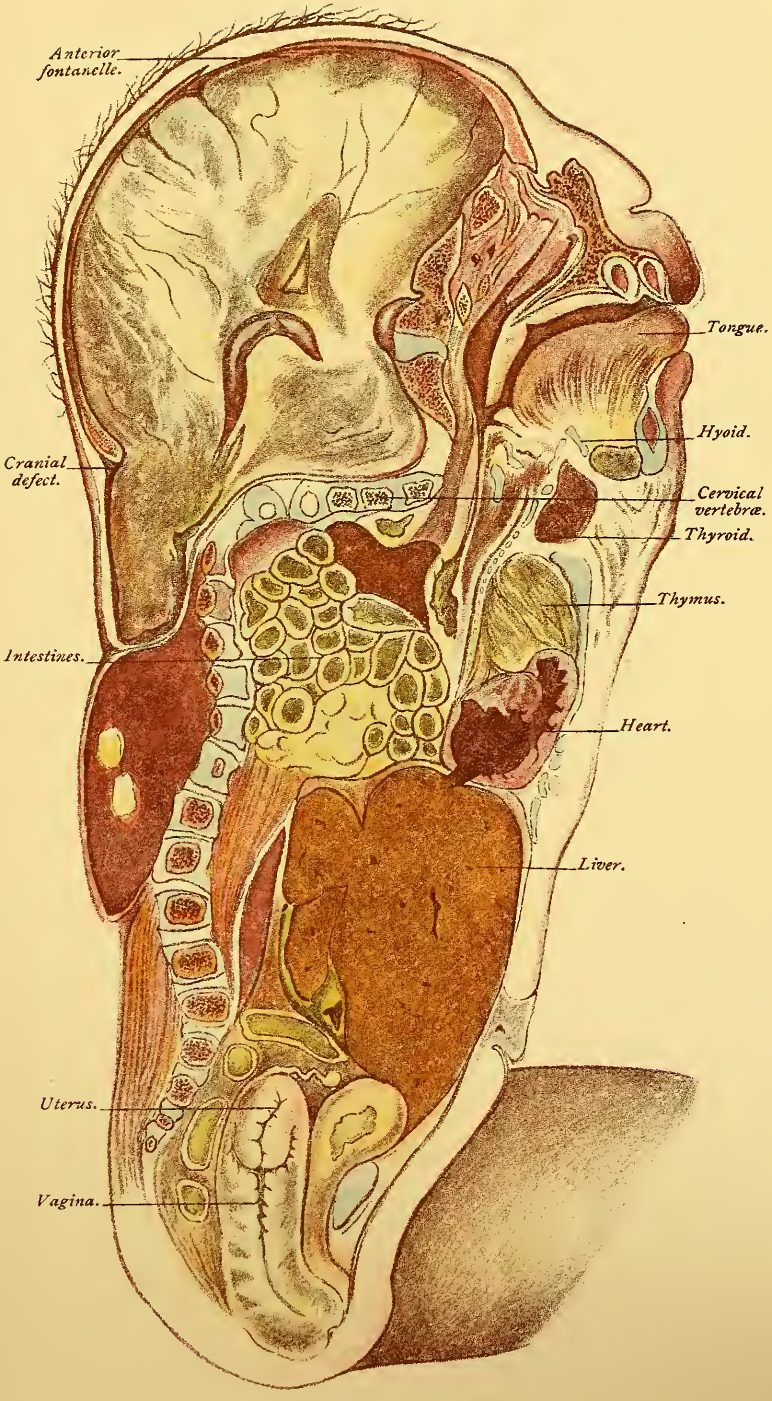


Fig. 46.—External Appearances of small Iniencephalic Fœtus. Specimen No. 277.

Two specimens, showing in an even more marked fashion the chief characters of iniencephaly, were examined by me by the sectional method in 1899 and 1900. One of these (Specimen No. 251)


Anterior fontanelle.
Tongue.
Hyoid.
Cranial defect.
Cervical vertebræ.
Thyroid.
Thymus.
Intestines.
Heart.
Liver.
Uterus.
Vagina.

was given me by Dr. William Fordyce. It was the product of the sixth gestation of a woman (thirty-five years of age), who during pregnancy had suffered from enormous distension of the abdomen; labour pains came on at the eighth month, and Dr. Fordyce ruptured the membranes, turned, and delivered the iniencephalic female fœtus shown in Fig. 48. Its length from vertex to perineum was 8½ inches, and its weight 1470 grms. Plate XVI. exhibits the sectional appearances: the head, again, is sharply fixed backwards, the occiput is manifestly defective, and there is spina bifida in practically the whole length of the vertebral column. It is to be noted that the brain lies partly upon the cervical and dorsal vertebral bodies and partly upon a spina bifida sac; the spina bifida sac, in its turn, rests upon the lumbar vertebral bodies. The spine showed cervical lordosis and dorso-lumbar cyphosis; there was also a lateral distortion; and several of the vertebræ were absent. On account of defective development of the diaphragm, several intestinal coils lay in the thoracic cavity behind the heart. The other specimen (No. 225) was given me by Dr. James Wilson in April 1899. It was the product of the second pregnancy of a healthy woman; her previous gestation, however, had ended in abortion at the third month. During the first two months of the present pregnancy there had been great sickness; there had also been remarkable constipation (a life-habit with the patient); and there had been much thirst, both during the day and at night. The fœtus, a small prematurely-born male, had a very thick umbilical cord, and a normal-looking placenta (Fig. 49). The frozen section (Plate XVII.) showed the usual sharp retroflexion of the head so characteristic of iniencephaly. The basis cranii looked directly backwards; there was cervical lordosis with compensatory dorso-lumbar cyphosis and some torsion; but the specimen differed from those already described in the fact that there was only a localised cervical spina bifida of short extent. Through a defect in the occiput, the cranial cavity communicated with a meningo-encephalocele which constituted a sac resting upon the closed part of the spinal column. In the cervical region, however, a small part of the brain lay upon the spinal cord in the open cervical part of the spine.

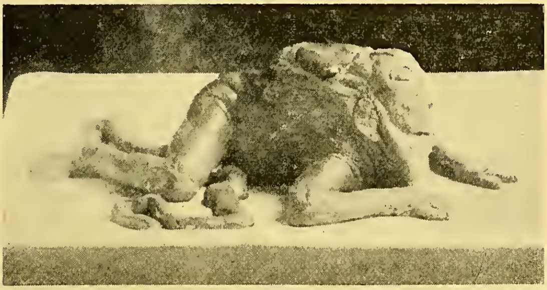


Fig. 47.—External Appearances of small Iniencephalic Fœtus. Specimen No. 162.

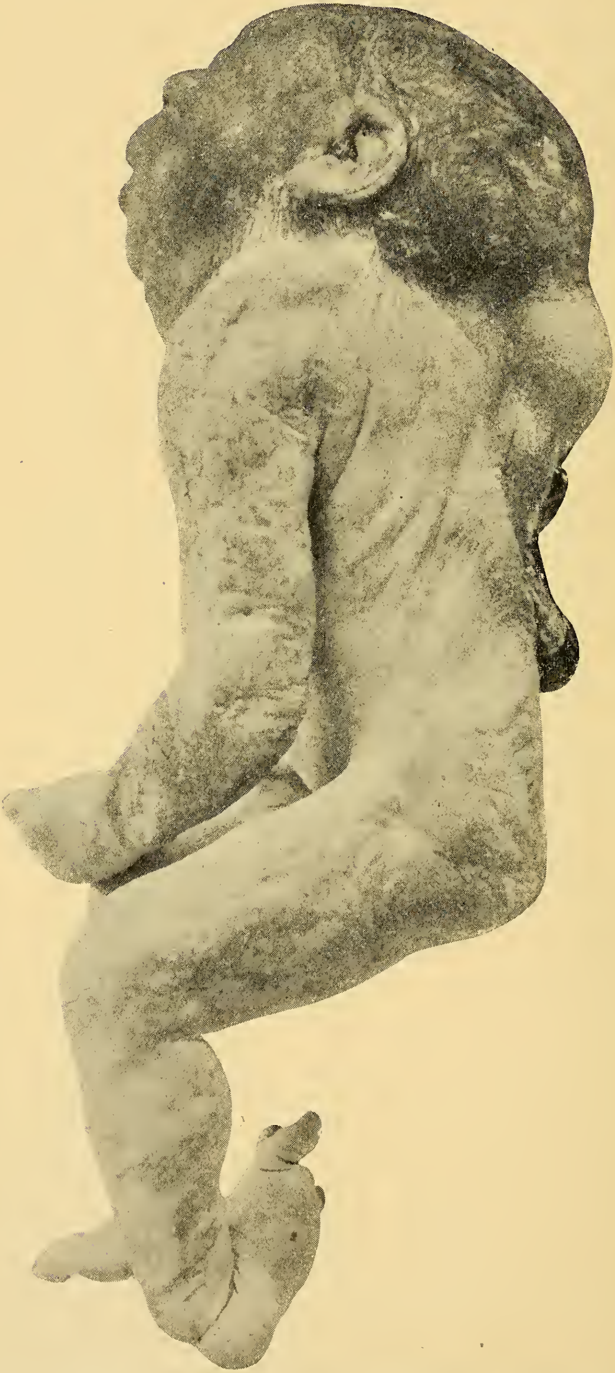
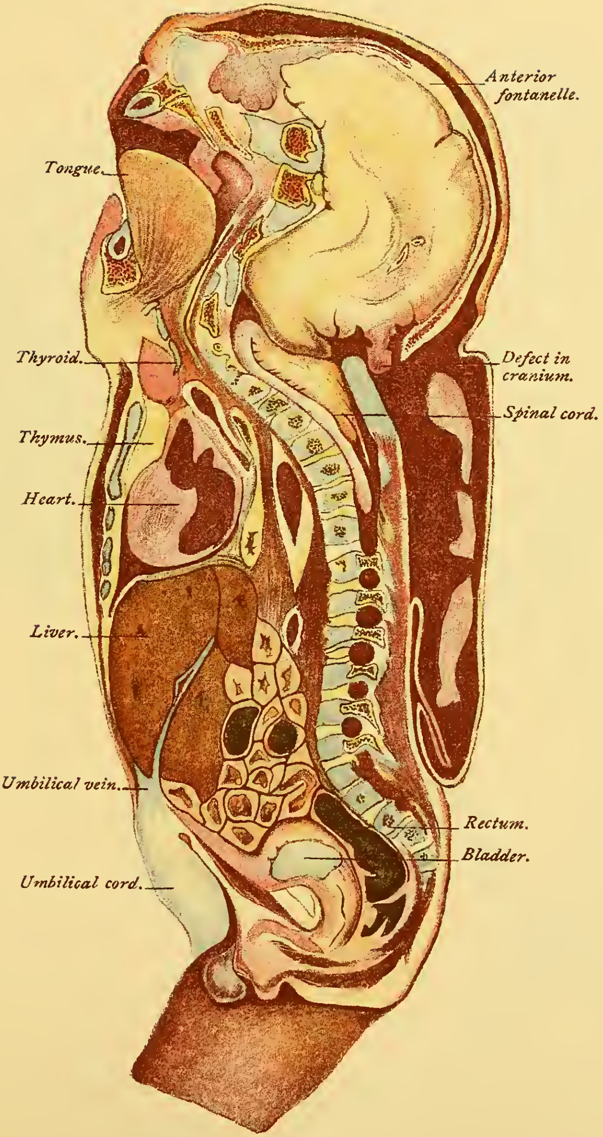


FIG. 48.—External Appearances of Iniencephalic Fœtus. Specimen No. 251.

PLATE XVII


Anterior fontanelle.
Tongue.
Thyroid.
Defect in cranium.
Spinal cord.
Thymus.
Heart.
Liver.
Umbilical vein.
Rectum.
Bladder.
Umbilical cord.

This specimen, therefore, had an unusual interest, for it exhibited iniencephaly unassociated with an extensive spina bifida, and presented the extraordinary picture of two separate portions of the brain lying posterior to the spinal cord in the cervical and upper dorsal region. The external appearances of this fœtus are represented in Fig. 49.

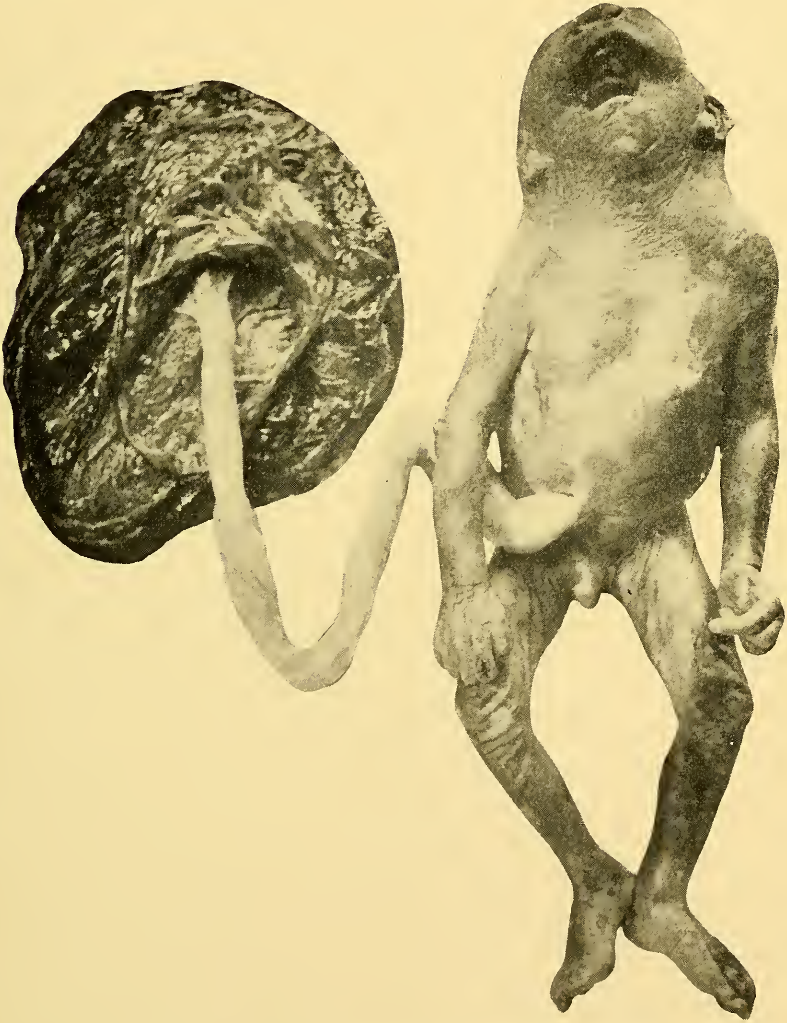


Fig. 49.—External Appearances of Iniencephalic Fœtus with Placenta. Specimen No. 225.

The reader will have gained some ideas of the morbid anatomy of iniencephaly from the descriptions of cases which I have given above. Let me note some additional points gathered from other records. The neck-groove is generally absent both anteriorly and posteriorly, but, sometimes, as in Lop and Pujol's specimen (5), it is indicated in front. In this case, also, there was not simply retroflexion of the head on the trunk, but the occipital bone was actually fused with the vertebral column at the level of the seventh dorsal vertebra; most of the cervical vertebræ were absent, and, through the bifurcation of the upper part of the dorsal portion of the spine and its fusion with the occiput, the first six pairs of ribs seemed to arise from the basis cranii. H. F. Lewis (6) collected together twenty-two cases of iniencephalus, including three described by himself. He divided them into two groups. In the first group were the cases in which the cephalo-rachidian cavity formed by the bending back of the head was complete, and contained the whole brain; this type Lewis termed *inienecphalus clausus.* To the second group he gave the name of *iniencephalus apertus,* and included in it all the specimens in which there was a small or large encephalocele, some of the cranial contents lying outside the cephalo-rachidian space. In this group we see the curious spectacle of part of the brain lying not only outside the proper cranial cavity but actually outside the new cavity formed by the cranium and the open spinal canal. One of Lewis's specimens was a male twin; nearly all the others seem to have been females and the result of single pregnancies. In a majority of the cases the mother was a primipara; but this is probably an accidental result, which more extended statistics might reverse.

The defect in the occiput varied considerably in individual instances. In Leith Napier's specimen (7), the basi-occiput as well as the squamous part was absent, and the basi-sphenoid bounded the much enlarged foramen magnum anteriorly; in Remfry's case (8), however, the basi-occiput and the ex-occipitals were developed, while the squamous part was represented by two crescentic curved plates of bone with a large opening between them. In Remfry's case, also, the curious anomaly was observed of the origin of part of the gluteus maximus (of the left side) from the left upper part of the defective occiput. A good diagrammatic sketch of the relation of parts in a typical iniencephalus is given by W. Hoffmann (9); in this instance the two rudimentary bones representing the occiput were separated by a distance of 4 cms. The spinal defect varied considerably in extent, being limited in some instances (as in my specimen No. 225, Plate XVII.) to the cervical region, and in others affecting the whole column. In most of the cases some vertebræ are absent. The altogether peculiar character of the spinal defect in iniencephaly is that the open canal produced by the want of development of the laminæ and spinous processes is closed in again by the retroflexed head and the skin covering it and extending to the sacrum.

Other malformations may be associated with iniencephaly: diaphragmatic hernia would seem to be one of the commonest of these; exomphalos, umbilical hernia, hydrocephalus, cyclops, horse-shoe kidney, and club-foot have also been noted.

Attempts to explain the origin of iniencephaly have, as usual, followed the lines indicated in the chapters on Teratogenesis. Reference has been made to maternal impressions by some writers, to pressure, uterine or intra-uterine, by others, and to the amnion by yet others. Amniotic pressure is probably the active cause; but in order to understand the *modus operandi*, it is necessary to take into account the normal mode of development of the head and spine of the embryo. If the reader will refer back to Chapter III. and look at Fig. 12 (p. 34), he will see that there is a stage of ontogenesis, corresponding to the third week, in which there is a normal retroflexion of the embryo corresponding to that found in iniencephaly. Under ordinary circumstances, that embryonic retroflexion is quickly replaced by the attitude of the fourth week (Fig. 13); but it is comparatively easy to understand how, if the bending of the spine be fixed, the iniencephalic state is produced. Let us suppose, for instance, that uterine pressure or more probably amniotic pressure (due to non-development of the amnion) is brought to bear upon the retroflexed embryo: the spinal curves will be retained and exaggerated; as the head develops, the occipital part will find its expansion hindered by the adjacent spine and the spine will have its closure posteriorly checked by the occipital part of the head, and in neither of these parts will ontogenesis be able to pass on to completion. It is quite possible that retroflexion may be produced at other periods in embryonic and fœtal life, and it may then be due to a short umbilical cord or to the entire absence of the cord (Duncan and Hurry, 10); but the anomaly so caused will not be iniencephaly. If the view that this monstrosity is due to the retention and exaggeration of a state of matters which is normal at the third week be true, then we ought to find in early abortion-sacs some evidence of it. This evidence, I think, we do obtain in such a specimen as that of C. B. Lockwood (11), which was regarded as about fifty days old and which showed retroflexion of the body and defective development of the cartilaginous spinal column.

It must, of course, be remembered that retroflexion of the fœtus and iniencephaly are not one and the same monstrosity: there may be retroflexion of the spine with no other anomaly, the fœtus being born with the head bent back and the limbs also lying behind the trunk, but with no other malformation (12); or there may be anencephaly with retroflexion (Fig. 28, p. 173), and this may or may not be conjoined with exomphalos; or, again, there may be exomphalos, without anencephaly, and with retroflexion (13). It is the defective state of the occiput and the condition of spina bifida, which, together with the retroflexion of the whole embryo, produces iniencephaly. Which of these anomalous states is primary does not, I think, matter very much: there is a stage in development when they are all normally present, and this stage, which ought to be very transitory, is permanently fixed and maintained in iniencephaly. Further ontogeny is hindered and cramped, and so the associated malformations (*e.g.* diaphragmatic hernia) arise.

Literature.—(1) I. G. Saint-Hilaire, *Histoire des anomalies*, ii. 310, 1836. (2) J. W. Ballantyne, *Trans. Edinb. Obst. Soc.*, xviii. 226, 1893;

Teratologia, ii. 88, 1895. (3) J. W. Ballantyne, *Teratologia*, ii. 287, 1895. (4) J. W. Ballantyne, *Trans. Edinb. Obst. Soc.*, xxi. 55, 1896. (5) Lop et G. Pujol, *Rev. obstet. internat.*, ii. 145, 1896. (6) H. F. Lewis, *Amer. Journ. Obstet.*, xxxv. 11, 1897. (7) L. Napier, *Trans. Obst. Soc. Lond.*, xxxvi. 116, 302, 1895. (8) Remfry, *Trans. Obst. Soc. Lond.*, xxxvi. 227, 1895. (9) W. Hoffmann, "Zwei Fälle angeborner Difformität," *Inaug.-Diss.*, Erlangen, 1883. (10) J. M. Duncan and J. B. Hurry, *Trans. Obst. Soc. Lond.*, xxvi. 206, 1885. (11) C. B. Lockwood, *Trans. Obst. Soc. Lond.*, xxix. 234, 1888. (12) R. M. Murray, *Trans. Edinb. Obst. Soc.*, vii. 59, 1882. (13) A. R. Simpson, *Trans. Edinb. Obst. Soc.*, vii. 80, 1882.

CHAPTER XVII

Merosomatous Terata (*cont.*): Malformations affecting the Spine; Spina Bifida or Rhachischisis; Synonyms; Varieties; Holo-Rhachischisis; Mero-Rhachischisis; Spina Bifida Occulta; Localised Rhachischisis without a Sac; Spina Bifida with Rachicele; Morbid Anatomy; Teratogenesis; Treatment; Bibliography.

Spina Bifida (Rhachischisis).

As the outstanding feature in the ontogenesis of the spine is the gradual closure of the medullary canal to form the central canal of the spinal cord and the gradual growth round the closed cord of mesenchymatous masses (derived from the sclerotomes of the mesodermic somites) to build up the vertebral column; so the commonest and most typical teratological state of the spine is an open condition of the vertebral canal, and sometimes also of the spinal cord, the result of the imperfect performance of this piece of organogenesis. The details of the process of chondrification of the sclerotomes to form the cartilaginous framework of the spine are not well known in the human subject; this is doubtless the reason why there are some parts of the teratogenesis of spina bifida which are obscure. Speaking generally, however, it may be said that the backward and inward growth of the laminæ (of one or of several vertebræ) is arrested and a wide or a narrow space is left unclosed in the posterior wall of the spinal canal. Through this opening, as a rule, a larger or smaller portion of the spinal contents (membranes and cord, in a more or less altered state) protrude, to form a tumour in the dorsal region. Such is, stated very generally, the idea that is to be formed of spina bifida and its mode of origin.

Synonyms.

In the *Observationes Medicæ* of Tulpius (1) there is the record of a case of "Spina dorsi bifidi," which from the accompanying description and illustration was evidently an example of lumbo-sacral rhachischisis; the name "spina bifida" thus given to the anomaly some two hundred and sixty years ago is still that by which the malformation is best known at the present time. The term, in its etymological sense, emphasises the state of imperfect closure of the vertebral canal; but in common use it has come to be applied also to the tumour or swelling (consisting of the spinal membranes with or without the cord) which projects through the opening. These two anatomical characters, the divided spine and the protruding swelling, are found in all the synonyms which have been proposed. "Rhachischisis" (2), for instance, emphasises the former character; while "spinal hernia" and "rachicele" direct attention specially to the latter. The term "hydrorrhachis" refers to the fluid contents of the sac; and the names meningocele, myelo-meningocele, and myelo-cystocele indicate the component parts of the sac. The defect in the spine and the protrusion of the spinal contents through it are commonly but not constantly associated: there may thus be spina bifida or rhachischisis in the strict sense of the words without rachicele or spinal hernia, and to this kind of case the name spina bifida occulta has been given; on the other hand, a hernial protrusion which at one time has been in communication with the interior of the spinal canal may afterwards be cut off therefrom, and so give rise to a tumour which is often classed simply as a "sacral cyst."

Varieties.

In naming the synonyms of "spina bifida," I have incidentally referred to some of the varieties of the malformation and to some of the structural peculiarities of these varieties; but it is necessary now to consider these matters more in detail. The following classification of the varieties may be adopted:—

I. Holo-Rhachischisis or Total Spina Bifida: the whole canal is widely open and there is no sac.
II. Hemi-Rhachischisis, Mero-Rhachischisis, or Partial Spina Bifida.
  A. Spina Bifida Occulta or Crypto-Mero-Rhachischisis.
  B. Spina Bifida without Spinal Hernia: the canal is widely open at one or more places, but there is no sac.
  C. Spina Bifida with Rachicele (common variety).
    1. Meningo-myelocele (common sub-variety).
    2. Meningocele.
    3. Myelo-cystocele, Syringo-myelocele, or Myelocele (Taruffi).

Not a little difficulty has been introduced into this subject by want of care in the naming of the varieties; hasty identification of a given case with one described by another writer in another language is perhaps in large measure responsible for this. Bland-Sutton (3), for instance, applies the term "myelocele" to a condition differing (as it seems to me) from that described by Taruffi (4) under that name; Taruffi, again, blames the English writers for giving the name "syringo-myelia" to cases of "myelocele," while the word they really used was "syringo-myelocele." Some of the confusion thus introduced is, I fear, almost irremovable; I can only endeavour not to add more to it. I shall describe each of the varieties of spina bifida named above, but I shall group most of the information round that known as meningo-myelocele, for that is, as it were, the central type.

Holo-Rhachischisis.

Under the name "Holo-Rhachischisis" may be conveniently grouped all these cases in which the whole spinal canal from end to end is open, in which all the vertebral arches are imperfectly developed. According to Taruffi, the first case of this kind to be described was that reported by P. Zacchia in 1661 (5), and since then many specimens have been noted. As a general rule, this widespread defect of the vertebral arches is conjoined with anencephaly, the cerebro-spinal canal being then open from end to end (*vide* Plate XXI., Fig. 50). There are a few exceptions to this rule, in which, although the spinal part of the canal is open, yet the cranial part is closed (save only in the occipital region); and these exceptional cases have been described in the previous chapter (*vide* Fig. 45) under the name of "iniencephaly." They are really instances of spina bifida occulta in its most extreme form. But the common type of holo-rhachischisis is that associated with anencephaly. In it, as may be seen in Plate XXI. and also in Fig. 50, the open spinal canal is continuous with the broad gutter or furrow on the basis cranii. The total number of vertebral bodies is generally diminished, and those in the cervical region show marked lordosis. The vertebral arches not only fail to unite posteriorly, they are turned outwards and so produce the wide groove or gutter which traverses the middle line of the back. This gutter is covered, it is stated, with the ventral portion of the dura mater, and possibly also with the corresponding part of the pia mater; in it may be found some strands of nerve tissue representing the spinal cord or a bifid cord in an atrophic state. Traces of the ganglia and spinal nerves may be found. Sometimes the bifid condition of the spine may extend to the bodies as well as to the arches, as in Lallemand's case (6) in which the first thirteen vertebræ were thus divided, the œsophagus finding lodgment between them. This was also the state of matters in the case reported by Cleland (7). It was one of holo-

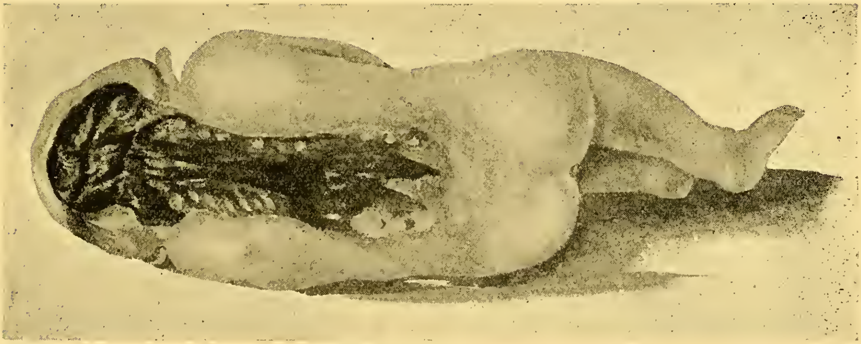


Fig. 50.—External Appearances of Fœtus with complete Spina Bifida and Anencephaly. Specimen No. 6.

rhachischisis and anencephalus in an embryo measuring $\frac{2}{3}$ inch in length; there were ragged and torn walls round the open neural canal, which Cleland interpreted as the burst walls of a dropsical sac and regarded as confirmation of the view that anencephaly and spina bifida are due to dropsical distension of the cerebro-spinal tube. They are capable of this interpretation; but they may also be explained as due to adhesions to the amnion or chorionic sac, for the early embryo described by Knoop (8) was attached to the chorion by its back. These questions, however, are more properly considered later, as are also the appearances, naked-eye and microscopic, of the spinal cord in such cases.

Mero-Rhachischisis.

Under the names "Mero-rhachischisis," "Hemi-rhachischisis," "incomplete spina bifida," and "localised spina bifida" are grouped all the cases in which the defective development of the vertebræ affects only a part and not the whole of the spinal column. These malformations are of more general interest, for they are not incompatible with postnatal existence, and some of them indeed may only be accidentally discovered in adults; holo-rhachischisis, on the other hand, prevents any but the most fleeting extrauterine life. It is also a comparatively common anomaly, occurring about once in a thousand births. If club-foot be reckoned as the most frequent of all the malformations, then spina bifida may perhaps be placed second in frequency.

In mero-rhachischisis the defect in the spinal canal may be unaccompanied by any protrusion of its contents, or it may be associated with a more or less marked swelling, consisting of the membranes of the cord or of the cord itself, or of both. In the cases in which the anomaly is unaccompanied by a swelling, the aperture in the spinal canal may be small and the skin and subcutaneous tissues may bridge it over and leave no external sign of the defect; or, on the other hand, the canal may be completely open, presenting simply a groove or gutter. To cases belonging to the former category the name of spina bifida occulta has been given; while those of the latter group may be termed localised rhachischisis without hernial protrusion. A short description of these two types of mero-rhachischisis must suffice.

Spina Bifida Occulta.

Masked spina bifida and crypto-mero-rhachischisis (Taruffi) are names which have been given to the cases in which there is no obvious external evidence of the defective state of the vertebral canal: there is no solution in the continuity of the skin covering the imperfectly ossified area, and there may be no swelling. This peculiar anomaly seems to have been first definitely recognised by Virchow (9) in 1875, although there were records of cases of it anterior to this year (10, 11, 12). Many instances have been reported in recent years. In some of the cases it was found that the skin covering the defect in the spinal canal carried a tuft of hairs often of considerable length (14, 15, 16, 17, 18, and 19); but although this association is common it is not constant, for in A. H. Dodd's case (20) there was no spina bifida and yet there was marked lumbar hypertrichosis, and in L. Mayet's patient (21) there was no sign of any defect of the vertebræ. On the other hand, there may be spina bifida occulta without hypertrichosis, as in the instances noted by Kirmisson (22), Bohnstedt (23), and others. At the same time, the discovery of lumbar or sacral hypertrichosis ought always to lead to a careful examination of the underlying part of the spinal column. In other forms of spina bifida, there is also a tendency to the development of hairs, and then they are usually arranged round the sac.

Spina bifida occulta commonly affects the lumbar part of the spine, but it may also be met with in the sacral region or in both lumbar and sacral regions. In quite exceptional cases it is situated in the dorsal region (as in one of Bland-Sutton's specimens, 24). The skin surface over the spina bifida may show either a depression or dimple or a slight elevation; and it may, as has been stated, be covered with hairs, often of considerable length and sometimes extending to the neighbouring parts (buttocks, loins). The opening in the spine may be quite palpable, and may involve the spinal processes and laminæ of three or four vertebræ; or it may be little more than a small fissure in the arch of one vertebra, when it may easily be passed over unobserved. In a case reported by Taruffi (25) there was no defect in the bone, but the ligamentous structures were absent. When there is an aperture in the arches, it is commonly closed by fibrous membrane, but the closure may be incomplete, allowing the subcutaneous tissue and fat to enter the canal. Further, a pad of fat may lie over the opening and conceal it; and in Lindsay's case (26) the diagnosis between spina bifida occulta and congenital lipoma remained doubtful. The spinal cord may be lengthened, reaching a level in the spine which it usually attains only in embryonic life (the tip of the coccyx in Bland-Sutton's case, 24); and opposite the defective arches and spines the central canal of the cord may be dilated, but there may be a degree of meningocele as well as of myelo-cystocele.

Some interesting anomalies in the vertebræ adjoining the defective ones may be met with. Half vertebræ, for instance, have been found; and curious false joints in the laminæ behind the position of the future articular processes have been discovered (24). The whole spine, also, may show marked curvature, lordosis, or, more rarely, cyphosis; and the spinal canal may be wide (23). The coccyx may be shortened or absent (22). Club-foot is a not uncommon complication; and the association of this anomaly with lumbo-sacral spina bifida occulta and a tuft of hair in the position of a tail has suggested to Bland-Sutton (3) that perhaps the idea of fauns and goat-footed satyrs had origin in the observation of such malformations. Other concomitant teratological states may be exomphalos (11), atresia ani, pharyngeal imperforation, absence of one kidney, fibrous changes in the appendix vermiformis (24), congenital dislocation of the hip (18), and dermoid tumours in the neighbourhood of the spinal defect or a fibro-myo-lipoma in the canal itself (Recklinghausen).

Unlike other varieties of spina bifida, the occult type does not prevent postnatal existence; but some paralytic phenomena and some atrophy of the lower limbs may result, and in adult life perforating ulcers of the feet or buttocks (66) may develop and lead to anxiety. Thus, in a case reported by Mr. Jones (27), the patient showed no abnormal signs till the age of seventeen years; then he developed paralytic symptoms and perforating ulcers of both feet; the spine was trephined in the region of the second sacral vertebra to relieve the pressure on the cauda equina due to a fibrous band, and the result was satisfactory. It is seldom, however, that operative interference is required in spina bifida occulta (28).

The theory of the causation of the masked variety of spina bifida can hardly be considered apart from that of rhachischisis in general (*q.v.* p. 302); but it may be stated here that there is some evidence that spina bifida occulta is really an ordinary spinal meningocele or myelo-cystocele which has undergone Nature's cure during intra-uterine life. It is thought that the meningeal protrusion has gradually re-entered the spinal canal, and cicatricial tissue partly or wholly closed the aperture, and this is not out of keeping with the state of the spinal membranes (absence of dura mater) and the presence of a cutaneous cicatrix in some instances. At the same time it must be remembered that great obscurity surrounds all the processes of intra-uterine repair, and especially with regard to the power of the parts to form structures at a late date which ought to have been developed early. Much has been written and speculated regarding the cause of the frequent association of hypertrichosis with this form of spina bifida, but without shedding any appreciable light; and the same must be said of the hypotheses advanced to explain the heterotopic presence of various tissues (muscle, fat, etc.) within the spinal canal (13, 23). Both these matters, however, seem to me to point to marked vitality of the surrounding structures, although the vitality has anomalous effects; herein may lie a hint as to the nature of the reparative processes.

Localised Rhachischisis (without Hernial Sac).

In Holo-Rhachischisis the spinal canal was open from end to end, and showed very rudimentary traces of either the cord or its membranes; the type at present being described resembles it in the complete openness of the canal and in the state of its contents, but the anomaly is localised in extent, affecting only one region of the back. Both types are generally associated with grave cranial defects, such as anencephalus or mero-acrania. The spinal defect may be in the cervical region, and then there is produced the variety of anencephaly known as derencephaly; the spines and laminæ of the cervical vertebræ are absent, the bodies are exposed, and the cord begins in the dorsal region. Again, the canal may be closed in the dorsal region and open in the lumbar or lumbo-sacral (Fig. 51). It may,

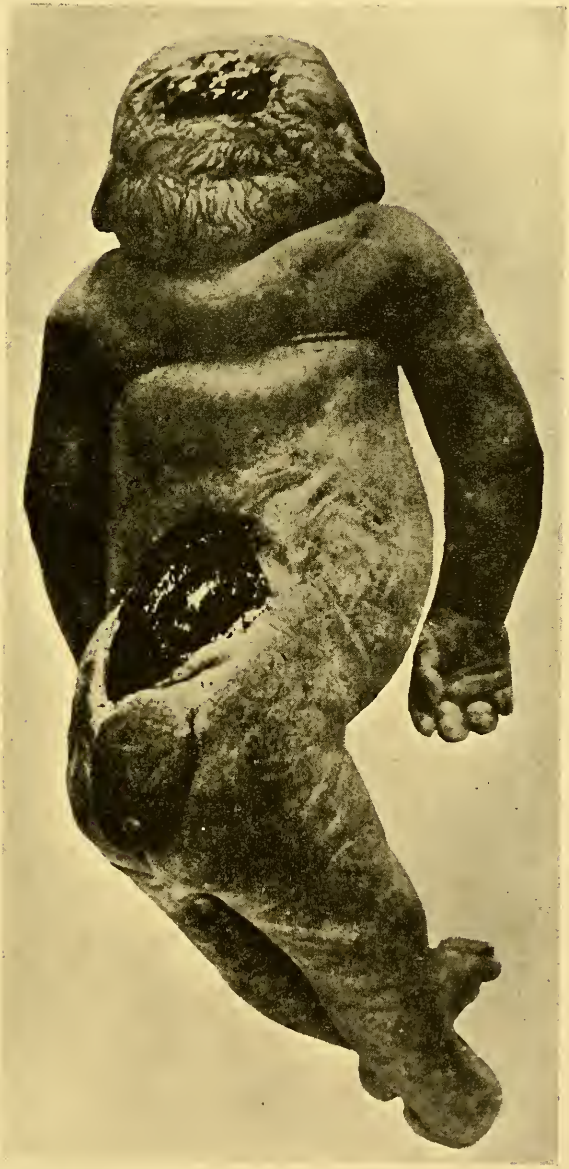


Fig. 51.—External Appearances of Fœtus with Lumbar Spina Bifida, Mero-acrania, Caudal Projection, and Anchylosed Joints. Specimen No. 113.

however, sometimes be difficult to determine whether in these cases a hernial protrusion may not have existed and then disappeared, being ruptured in labour. At any rate, the malformation is not compatible with postnatal life. I have met with several instances of it in association with anencephaly (*vide* Plate XXII.), generally in the cervical region but sometimes in the lumbar; in one case (Fig. 51) I found it coexisting with defective ossification of the anterior and upper part of the cranium.

Spina Bifida with Rachicele.

Spina Bifida with Rachicele (hernial protrusion of the contents of the spinal canal) now falls to be described. It is the form which is usually meant when the name Spina Bifida is used without qualification. It is also compatible with a certain length of life after birth, and it is often made the subject of surgical interference. It has, therefore, a high importance and calls for a detailed description. There are three varieties of it, according to the composition of the rachicele or hernial protrusion: these are myelo-meningocele, meningocele, and myelo-cystocele. There are also varieties according to the region of the spine affected (cervical, dorsal, lumbar, or sacral), and according to the part of the circumference of the spinal canal left open (posterior, lateral, anterior). The whole subject is a large one, and I must economise time and space; I shall, therefore, try to concentrate the attention of the reader upon its antenatal aspects, leaving the description of clinical postnatal phenomena and competitive plans of operation to the Surgery Text-books. For more elaborate details of the pathological characters of the malformation reference may profitably be made to the classic articles of W. Koch (29), F. von Recklinghausen (13), and to the Report of the Committee of the Clinical Society of London (30).

Morbid Anatomy.

In presenting the morbid anatomy of Spina Bifida I shall first deal with the structural peculiarities of the vertebral column, then with those of the contents and of the hernial protrusion, and finally with the commonly associated malformations in the cerebrum and elsewhere.

1. *The Spine.*—The region most often affected with spina bifida, as Ruysch (31) pointed out long ago, is the lumbar or lumbo-sacral, and next in order of frequency is the sacral; in about 77 per cent. of all cases the defect is either in the lumbar or sacral region or in both. Far less frequently is cervical spina bifida met with (it is even doubtful whether some of the cases of so-called cervical spina bifida were not, after all, instances of occipital meningocele); and dorsal, dorso-lumbar, and cervico-dorsal specimens are the rarities of Museums. The reason why the lumbo-sacral region is the commonest site of spinal fissure is probably the ontogenetic one, that there the medullary groove is latest in closing to form the neural canal. The 8 mm. human embryo described by Tourneux and Martin (32), in their important article, had a neural canal still

open in the lumbo-sacral region, and was regarded by Dareste (33), as an early instance of spina bifida without a rachicele; Tourneux and Martin, however, thought that if the embryo had lived on, the hernial sac would have formed; but the value of the specimen resided in the presence of the open canal in that position in so young an embryo.

In the great majority of cases the defective closure of the spinal canal is found in the middle line posteriorly; in two or more vertebræ the spinous processes are absent, and the halves of the laminæ do not meet, or are actually directed outwards, and therefore away from each other. "In extreme cases they are so everted as to lie in a transverse vertical plane" (30). Sometimes, however, the osseous defect is situated laterally; P. Hewett (34), Taruffi (35), and others have recorded instances of this, but it is rare. In Hewett's case it was associated with hydrocephalus and in Taruffi's with exomphalos; and in 1896 Mr. Cotterill (36) brought under my notice a boy, nine years of age, suffering from a spina bifida which protruded laterally through the sacrum through an opening opposite the right sacro-iliac synchondrosis, and showing in addition a number of minor malformations (congenital hydrocele and inguinal hernia, non-descent of testicle, etc.). Sometimes, again, the hernial protrusion may take place between the arches of two successive vertebræ, *e.g.* the fifth lumbar and the first sacral (37), or the seventh cervical and the first dorsal (38); this variety has been termed interstitial spina bifida. Yet again, the spinal defect may be situated anteriorly, affecting the bodies of the vertebræ; it may then be conjoined with posterior spinal deficiency, as in the case of Tulpius (1), or may exist alone, as in Kroner and Marchand's specimen (39). Anterior spina bifida existing alone may easily lead the surgeon into diagnostic and therapeutic error, as in the case (39) just referred to, where an intra-pelvic tumour (a sacral meningocele) in a young woman was regarded as a cyst of the broad ligament, and was twice tapped, with a fatal issue. In Emmet's case the sac resembled an ovarian cyst (40).

The vertebral column may show structural peculiarities other than those observed in the defective spinous processes, laminæ, and bodies. Certain vertebræ may be altogether wanting (Hauner, 41); or there may be half vertebræ, causing lateral distortion of the spine (Specimens 25 and 26 reported on by the London Committee, 30); and, perhaps in consequence of these anomalies, there is shortness of the whole vertebral column. A very striking and suggestive anomaly that has occasionally been found in spina bifida is the presence of osseous or cartilaginous processes from the posterior surface of the bodies of the vertebræ, which project into the spinal canal, and completely, or more often incompletely, divide it into two compartments. This condition may be accompanied by a more or less complete division of the spinal cord into two halves, each with a central canal (diastematomyelia). Instances have been recorded by Cruveilhier (42), Boullard (43), Houel (44), Humphry (45), the London Committee (30), Recklinghausen (13), Cleland (46), Taruffi

(47), and others. The anomaly may be associated with the presence of two centres in the body of one vertebra (30). One of these interspinal osseous projections is seen in Fig. 52, which represents the vertebral column of a case of spina bifida and commencing hydrocephalus examined by me in 1899. The exact significance of such growths is at present uncertain, but I have called them "suggestive," because of their possible bearing upon the causation of spina bifida (*q.v.*).

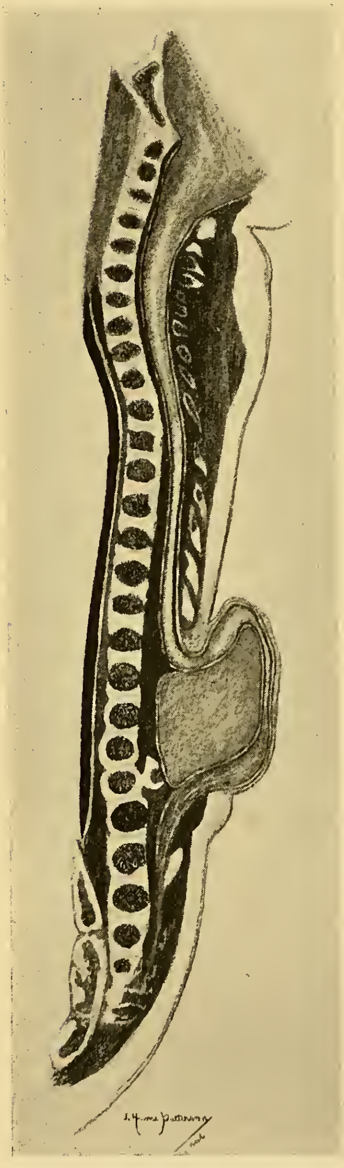


Fig. 52.—Spinal Column and Cord in a case of Spina Bifida (Specimen No. 233), showing new growth from third lumbar vertebra into spinal canal, which consisted of bone and cartilage.

2. *The Hernial Protrusion* (*Rachicele*).—In each case of spina bifida there is commonly one hernial sac alone, and that sac has only one cavity; to the latter rule there are, however, exceptions, and multilocular sacs have been noted by the London Committee (30) and others; in them the loculi communicated by small apertures. The swelling is usually rounded in form resembling a tomato (Fig. 53), but it may also be oval with the long axis running vertically; sometimes it is slightly flattened, and when it is multilocular the internal subdivisions may be indicated externally. A slight depression or umbilicus on the outside may point to the insertion of the spinal cord on the inside. In size the sac may be that of a pea or a bean, or that of a child's head or even larger (*e.g.* 25 inches in circumference); all intermediate dimensions may be met with. It may be sessile or pedunculated, and its pedicle may be broad or, less often, narrow. It may be covered by skin, but this is rather rare; the coverings usually consist of the more or less altered meninges, the skin stopping at the base of the swelling. When the skin is present, it may be thick and vascular and provided with a considerable adipose layer; and it may exhibit a ring of hairs or be surmounted by a tuft of them. Occasionally the skin is thickened and leathery (34), and sometimes the subcutaneous tissue is of a

myxomatous type, as in Matthews Duncan's case (48), and in one examined by Kirmisson and Berger (22). Generally, the skin, when it is present, is thinned out; and Béringier and Chambard (49) have given details of its histology, among which the disappearance of the subcutaneous fat and of the hair follicles and sweat glands is a conspicuous feature. When the cutaneous covering gets so altered it becomes difficult to distinguish it from the dura mater; and when the sac-wall is purely meningeal it may have an almost transparent appearance. This leads me to touch upon the most difficult point in the morbid anatomy of Spina Bifida, the composition of the sac-walls and sac, a matter deserving a new paragraph.

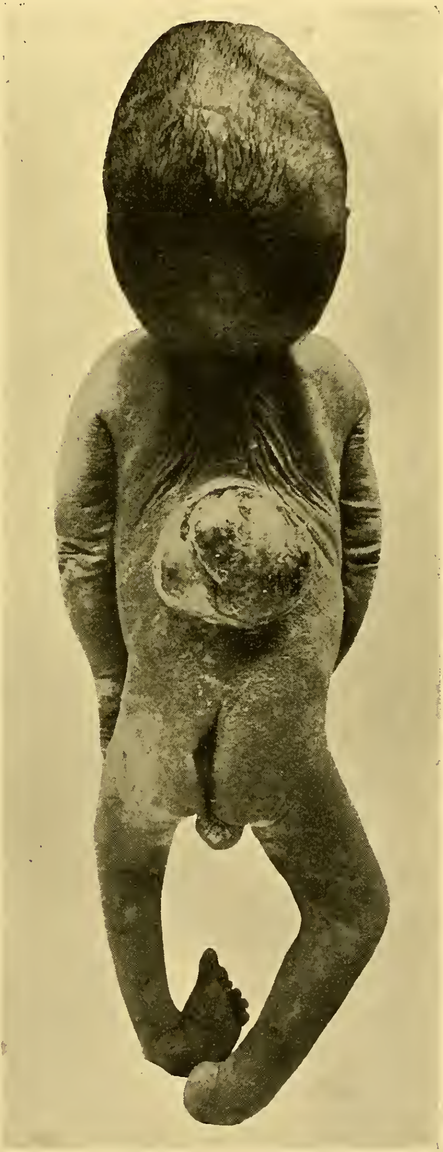


FIG. 53.—External Appearances of Fœtus with Lumbar Spina Bifida and Club Feet. Specimen No. 233.

The sac may consist simply of the spinal membranes (*spinal meningocele*). This form I describe first, not because it is the commonest but because it is the simplest; as a matter of fact it is a rare variety, representing about 8 per cent. of all spinal hernias (30). It is a local hernia of the membranes; the spinal cord itself is, as a rule, normal in position, but if the osseous defect be large there may be some prolapse of the cord or of its termination (cauda equina) into the sac. It probably more often occurs in the sacral than in the cervical region, for some of the recorded cases classified as cervical in position were no doubt occipital and not spinal meningoceles. It is exceedingly rare in the dorsal, and is only occasionally met with in the lumbo-sacral region. I have met with two instances of it, both in the sacral region (Figs. 29

and 54); when it is so situated the sac may protrude from the sacral hiatus and the coccyx be split into halves. The sac may be of all sizes, and it is not uncommonly very large when sacral in position.

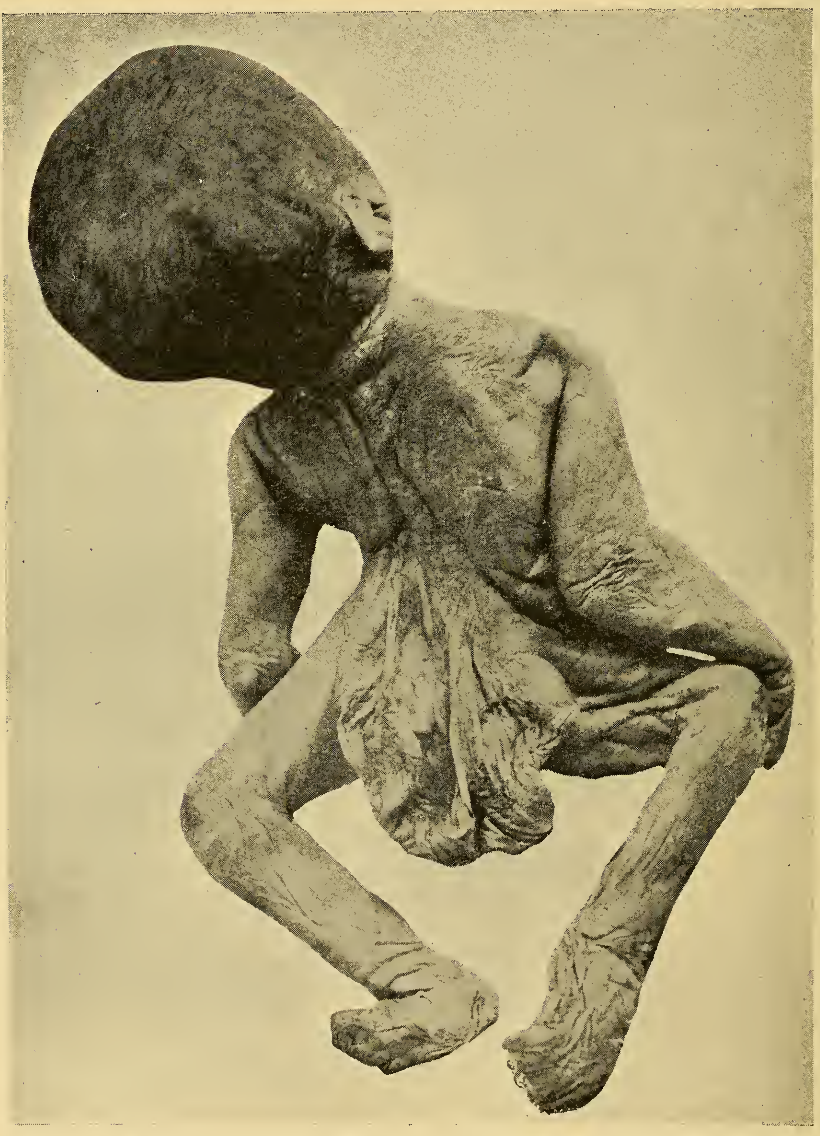


FIG. 54.—External Appearances, posterior view, of Fœtus with Sacral Spina Bifida, and Exomphalos and Ectopia Vesicæ. Specimen No. 200.

Its wall has been regarded as composed of the dura mater and the arachnoid; but Recklinghausen (13) and Muscatello (50) both believe it to consist of the arachnoid alone, often somewhat thickened.

The whole sac may be subcutaneous, or there may be a skinless area on its convexity; the membranes (or membrane) may be adherent to the cutaneous covering. The inner aspect of the sac-wall has the appearance of a serous membrane.

In the majority of cases of spina bifida, however, the hernial protrusion contains in its wall the flattened-out spinal cord itself as well as the membrane (*myelo-meningocele*). The fluid lies not between the membranes as in the former variety, but between the cord and its envelopes. The cord is commonly found flattened out in the posterior wall (Fig. 52); and that the cavity is not due to dilatation of the central canal of the cord is proved by the discovery of that central canal in an undilated state in the substance of the posterior wall of the sac (30). The spinal nerves pass forwards across the interior of the sac to the intervertebral foramina. Tourneux and Martin (51) have described the spinal cord passing obliquely from above downwards and from before backwards to penetrate the wall of the sac and to find lodgment between the membranes (arachnoid and dura) and the more or less altered skin; but Recklinghausen (13) has investigated very thoroughly a more common arrangement of parts. This latter observer has not found either the membranes (arachnoid and pia) or skin at the apex of the spina bifida sac; there he discovered only exposed spinal cord, or rather its remnants continuous with the cord above and with the filum terminale below. Myelo-meningoceles are common in the lumbo-sacral region, and according to Recklinghausen they exhibit at the apex a reddish velvet-like area (vasculo-medullary) made up of numerous blood vessels with nerve fibres and cells supported by the ventral pia mater; at the upper pole of this area is a small oblique funnel-shaped depression (infundibulum) marking the point of insertion of the cylindrical spinal cord within the sac; round the vasculo-medullary area is a thin smooth zone (epithelio-serous) formed by the pia mater and not covered by remains of nerves but by an epithelial stratum with a thin epidermic layer; and round this zone, again, is the skin of the back. The three zones are seen in Fig. 53, and a good coloured plate showing these areas is given by Bockenheimer (78). All myelo-meningoceles do not, however, show these characters. In some instances there is no velvet-like medullo-vascular area but only a smooth surface, like a congested serous membrane, constituted by the exposed pia mater with no nerve remnants, and to be accounted for perhaps by the action of the liquor amnii (13) or by the great degree of distension of the sac, especially if it correspond to a cyphotic curve of the spine (52). In other instances, the myelo-meningocele is covered entirely with skin; and in yet others with an epidermic layer, which possibly represents skin in an early stage of development. The cavity of the sac in myelo-meningoceles represents, therefore, the ventral part of the expanded subarachnoid space.

In a third group of cases the sac is constituted by an expansion of the central canal of the spinal cord (*myelo-cystocele*, *syringo-myelocele*). This is a rare variety of spina bifida, and is apt to be associated with marked spinal curvature (scoliosis, lordosis) and with such monstrous states as exomphalos and ectopia vesicæ (Fig. 54). Recklinghausen (13) and Muscatello (50) have especially investigated this type. In it the osseous defect is more often situated laterally than in the other two varieties. The sac is covered by the skin, subcutaneous fat, and aponeuroses; and the wall consists of the thin spinal membranes (without any trace of the dura mater), lined internally by cylindrical epithelium. The spinal nerve roots pass forwards at the sides of the sac, and are not found inside it; they lie between the inner lining membrane and the other layers of the wall. A meningocele may coexist with such a myelo-cystocele as has been described (54) and give rise to the compound myelo-cysto-meningocele; in it there is fluid not only in the dilated central canal of the cord but also in the subarachnoid space, dorsal or ventral. This third variety of spina bifida can only be distinguished from the first by dissection. The central canal of the cord may show dilatation above the level of the sac, but this in itself does not prove the sac to be a myelo-cystocele, for such dilatations may occur in other varieties of spina bifida and also apart from it altogether.

To summarise briefly the three varieties of sac, it may be stated that the spinal meningocele is simply a local herniation of the membranes, the cord being practically normal; the myelo-meningocele has a sac-wall composed of the membranes and the cord, which latter structure appears as if it has been flattened out and pressed against one wall of the sac and united with it; and the myelo-cystocele has a sac-wall made up of the cord and the membranes, the fluid accumulation being in the central canal of cord. In the two former varieties the fluid is outside the cord, in the third type it is inside the cord.

The fluid contents of the spina bifida sac have been analysed several times. W. D. Halliburton made three analyses for the Committee of the London Clinical Society (30), one of which is given here. The fluid was drawn from a lumbo-sacral sac in the case of a female infant eleven days old, and it was the first tapping.

Water	989·877	
Total solids	10·123	
Proteids (containing globulin)		1·602
Soluble salts		7·544
Insoluble salts		·346
Extractives		·631

The fluid was clear and faintly yellow in colour, had a slightly alkaline reaction, and showed a slight trace of sugar. The specific gravity is low (usually about 1007), and boiling produces an opalescence but no coagulation.

3. *The Spinal Cord and its Membranes.*—Not only does the spinal cord show anomalies of structure when it forms part of the spina bifida sac (as in myelo-meningocele and myelo-cystocele) but it may also do so in the simple meningocele; further, it may exhibit malformations in other parts of its extent than in the immediate neighbourhood of the spinal defect. I have already referred to the

condition of diastematomyelia, in which, especially in spinal meningocele, the cord divides into two strands, each with a central canal, and unites again into one band at a level below the sac; this state may or may not be associated with the presence of an osseous or cartilaginous projection into the spinal canal. Sulzer (55) describes fully a case of division of the cord in which such an exostosis existed, and refers at length to other cases of diastematomyelia; and Warrington and Monsarrat (56) give full details of another instance in which there was also arrested development of the cerebellum and hydrocephalus. In the latter case (56) the division of the cord and the exostosis were both situated in the dorsal region above the level of the spina bifida (which affected the fourth and fifth lumbar vertebræ); this would seem to show that the exostosis has not the teratogenic effect on the spina bifida which some writers have ascribed to it. Further, Theodor's observation (97) of a cord double from the third dorsal vertebra backward would seem to show that the duplicity was due to a wedge of grey and white matter pushing its way into the cord posteriorly and so separating the posterior columns; the central canal was also double, and these gave off several branches.

Apart from division of the spinal cord, other malformations of it may be present in cases of spina bifida. Dilatation of the central canal, for instance, has been noted; it is commonly situated above the level of the spina bifida. Hydromyelia, however, may occur quite apart from spina bifida, and it is not proven that it often has a causal relation to it; but sometimes the canal in the cord would seem to be continuous with the sac of the spina bifida (30). The cord itself may be normal in size, but often it is attenuated; it may end abruptly or be too long for the canal.

I have already referred to the difficult question of the arrangement of the membranes in cases of spina bifida. The difficulty seems to be largely due to the fact that in the sac-wall the membranes may be found in an undifferentiated state. Thus, in the posterior wall (in cases of myelo-meningocele) we may find the structures which normally precede and give rise to the spinal membranes: these structures, mesoblastic in origin, ought to be developed between the epiblast of the cord and that of the surface; but they either remain undifferentiated, or only advance to the stage of myxomatous tissue, or are absent altogether. In this way the peculiar relations of the cord to the surface may arise. At the neck of the spina bifida sac, however, it is generally possible to trace the membranes: the arachnoid, at any rate, can be seen there, and may be followed for a greater or less distance in the sac-wall. The dura mater, often in a congested state, may be recognisable anteriorly in connection with the bodies of the vertebræ; but, as a rule, it cannot be traced in the wall of the sac posteriorly. Both the pia mater and the arachnoid are commonly found thickened. Bockenheimer (78) gives useful although somewhat schematic representations of the supposed arrangement of the membranes in the different types.

4. *Complications.*—It would, of course, be out of place here to enter in detail into the morbid anatomy of the complications of spina

bifida; that would be to anticipate the description of many of the succeeding teratological types. At the same time, the commonly associated malformations of the brain deserve a few lines of description.

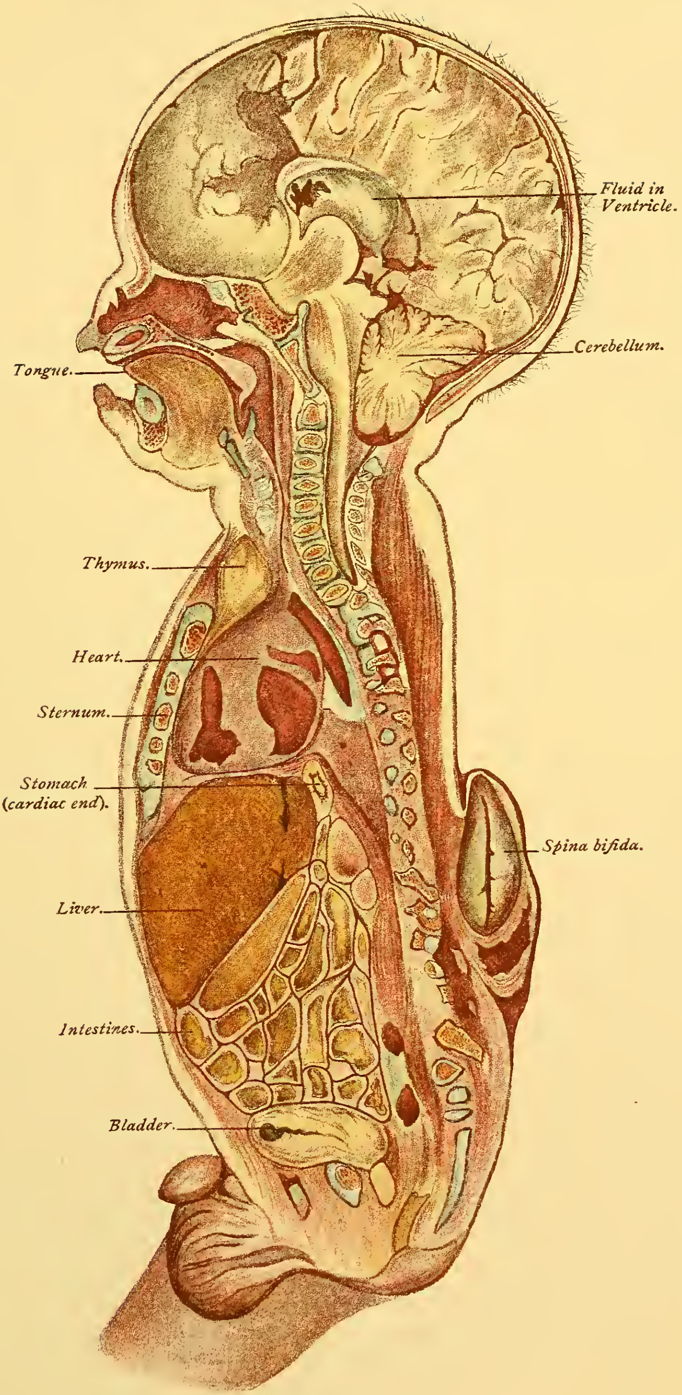
(*a*) *In the Brain.*—Hydrocephalus, as is well known, is a frequent concomitant of spina bifida. It may only become apparent after some operation upon the sac has been attempted; but, as Plate XVIII. shows, it may be present without there being any external sign of it at all, and before any active treatment has been initiated. This fact must be taken into account in deciding whether an operation should be attempted and at what time. The association of spina bifida and hydrocephalus is well shown in Specimen No. 246, represented in Plate XX.; in it the section has passed to the side of the middle line in the cephalic region, and, therefore, the distension of the lateral ventricle is well shown.

Anencephalus as a complication of spina bifida has been already referred to; but there are other changes in the brain besides those of anencephalus and hydrocephalus. In a painstaking and beautifully illustrated article, Nicolas Solovtzoff (57) has described five cases of spina bifida. From the examination of these specimens he comes to the conclusion that spina bifida is sometimes accompanied by dropsical enlargement of the fourth ventricle, leading to its elongation in a downward direction; this may be associated with downward displacement of the whole medulla oblongata, and in some instances the posterior part of the medulla is so displaced as to lie upon the spinal cord or to be united directly with it. The result of these changes was that the fourth ventricle, which normally can only be seen when the cerebellum is raised, was visible below the level of the latter structure; it was covered only by the valve of Tarin and a membranous expansion of the cerebellum.

The development of the cerebellum itself was defective in most of Solovtzoff's specimens (absence of the vermis, etc.). In my specimen (No. 233) shown in Plate XVIII., a somewhat similar displacement of parts has evidently taken place; the cerebellum and medulla oblongata are both at a lower level than is normal and the basis cranii looks backward in a marked degree. Gudden (96), also, has described a case of dorsal spina bifida in a human embryo, in which there was a remarkable swelling of the inferior vermiform process of the cerebellum, which projected into the fourth ventricle; the spinal cord at its origin from the medulla was bent upon itself, and near the spina bifida it divided into two parts.

(*b*) *Outside the Nervous System.*—Another complication which occurs not uncommonly in cases of spina bifida is the presence of *congenital neoplasms*, some of them of the nature of teratomata, others teratoid in character, and yet others more simple in structure; most of these tumours are attached to the sacrum and coccyx in the neighbourhood of the spinal defect. I have described a case (Specimen 113) in which a lipoma was situated in the gluteal region just below an open spina bifida (Fig. 51). Sometimes the growth has been found to communicate with the interior of the canal. I shall speak again of these sacral neoplasms.

PLATE XVIII


Fluid in Ventricle.
Cerebellum.
Tongue.
Thymus.
Heart.
Sternum.
Stomach (cardiac end).
Spina bifida.
Liver.
Intestines.
Bladder.

cicatrisation with a shrinkage of the sac and more or less complete cure, especially in meningoceles; at other times they consist in inflammatory processes which affect the cord and brain. The reader can, therefore, understand how difficult it is to recognise the individual spinal membranes and parts of the spinal cord in the spina bifida sac which has passed through the vicissitudes enumerated above.

Teratogenesis.

To attempt to describe the different explanations of the origin of spina bifida that have been advanced by various writers would simply be to tell over again the greater part of the story of the teratogenetic theories of the past and present already dealt with in an earlier part of this volume (pp. 107–224). I shall be brief.

There was, first, the theory of maternal impressions. It was never difficult to discover that at some time or other in her pregnancy the mother had seen a case of spinal disease, or had received a blow on the small of the back, or in some way had got a fright. In a case seen by myself in the Maternity Hospital in December 1903, the mother had had a fall from a car between the fourth and fifth month of pregnancy, and she was inclined to ascribe the spina bifida in her infant to that cause; but she had also had a severe illness (catarrh of the stomach and inflammation of the lungs) at the sixth month, and thought it might also have played a part. I believe the spina bifida was in existence long before either the fall or the illness occurred.

Then came, in their turn, the theories of traumatism and pressure. A blow on the mother's abdomen during her pregnancy might injure the fœtal back and so cause the spinal aperture, through which the contents would then protrude. A sharp curve in the vertebral column (and such curves are, as we have seen, associated with spina bifida) might by its mechanical action reopen the medullary canal; a cyphotic curve would specially tend to open the posterior part of the canal (76), and the cyphosis itself might be due to traction on the umbilical cord, from excess of the liquor amnii or disorderly fœtal movements, etc. (77). Although Lebedeff (76) and Marchand (77) both supported this view, Recklinghausen (13) has adduced arguments against it, among which is the fact that spina bifida may be found associated with lordosis as well as with cyphosis. At the same time there may be an element of truth in the theory, for the curves which are found in the spine of the fœtus when born may be different from those which were present when the spina bifida was being induced. The pressure of the amnion has also been invoked to explain the various forms of spinal defect and herniation; but the discussion of this possible factor is more correctly taken later.

Many pathologists have looked to disease of the cerebro-spinal nervous system as the cause of spina bifida. At first sight it is reasonable enough to believe that there is dropsical distension of the spinal cord or of its membranes, and that the consequent enlargement prevents the closure of the spinal canal; but there are difficulties in accepting the view, as we shall see. The association of hydrocephalus with spina bifida was early noted, and it was thought that the latter was due to the former; it was not clear what the sequence of events was, but it was conjectured that the cerebral ventricles (*e.g.* the fourth) might rupture, and so the contained fluid might make a way for itself down into the vertebral canal. Some cases seemed to favour this view, but in others no such communication could be found, and in them it was thought that the fluid had descended under the membranes, following what might be called natural routes. Morgagni (79) found it necessary to admit a spinal origin of the fluid in some cases, for otherwise it was impossible to account for the cases in which there was spina bifida without hydrocephalus; in other instances the cephalic origin might be allowed to exist, for in them rupture of the spinal sac caused shrinkage of the hydrocephalic enlargement. Morgagni's views held sway for some time, and they were rather strengthened by the inclusion of the idea of a dropsical distension of the central canal of the spinal cord (Portal, 80). But the variety of spina bifida in which the sac is due to distension of the central canal of the cord is, as we have seen, a rare one. Further, Cruveilhier (81) noted the independent occurrence of hydrocephalus and spina bifida, and had a difficulty in explaining the adhesion of the spinal cord to the meningeal sac (in meningo-myeloceles) by Morgagni's theory. Some modern authors, however, have not found such adhesions incapable of explanation. Tourneux and Martin (32), for instance, have ascribed them to the pressure of the fluid within the subarachnoid space; and Hofmokl's experiments (82) with a model of a spinal canal and cord seemed to support this hypothesis, although W. Koch (29) pointed out possible fallacies in them. Of late, however, the general trend of teratological opinion has been away from the theory that dropsy of the cerebro-spinal nervous system was the cause of spina bifida. Even Solovtzoff (57), whose observations demonstrated the presence of dropsical enlargement of the fourth ventricle along with a series of dislocations of the cerebellum, medulla oblongata, and cord, does not claim that there is a constant association of the spina bifida and the ventricular changes. At the present time the idea of diseased conditions of the brain and cord as causes of spina bifida has largely given place to that of arrested development; at best, it takes a subordinate place in the latter theory. To this view I must now direct the reader's attention; the theory of the action of the amnion is almost constantly combined with it.

What has been called the embryological theory in teratogenesis would seem at first sight to offer a real solution of the difficulty met with in the explanation of the origin of spina bifida. There is delayed closure of the medullary groove due to imperfect development of the medullary folds (due in its turn, perhaps, to amniotic pressure from maldevelopment), and so an open condition of the spinal canal is produced. This apparently simple explanation, however, does not account for all the facts. By the above-described mechanism we are able to explain the cases of holo-rhachischisis in which there is a wide vertebral groove or gutter with a layer of rudimentary nerve tissue covering it; in such instances there is evidently a want of closure of the medullary groove, and of all the later formed structures which lie posterior to it, including the laminæ and spines of the vertebræ. In other cases, however, such as those in which the spinal cord is present and contains a central canal, it is evident that the medullary groove has closed; in them the cause of the spina bifida would seem to lie in the imperfect differentiation of the tissues which are found between the spinal cord and the dorsal epiblast, including the membrana reuniens superior, which is the *anlage* at the corium, spinal laminæ, and membranes (Ranke, 83). For a time the spinal cord and the dorsal epiblast are in apposition, and then they are gradually shut off from each other by the mesodermic prolongations; it is easy to imagine how a defect in the ingrowing mesodermic plates would allow spinal structures to remain attached to epidermic ones, and so produce some of the varieties of spina bifida. Secondary factors may come into play as well as this primary fault in the mesoderm; individual vertebræ will be ill-developed, and thus bendings of the spine may be produced, and the canal become too short for its contained cord (Recklinghausen, 13).

Attempts have been made to arrange in series the varieties of spina bifida according to the stage in development when the arrest in ontogenesis occurred. Thus Bland-Sutton (3) has five types. In the first the medullary folds unite imperfectly, and this gives rise to what Bland-Sutton terms a *myelocele*, but is perhaps better distinguished as a simple *rhachischisis*; in the second the medullary folds unite throughout, but fail to separate from the surface epiblast, and the central canal subsequently dilates, *myelo-cystocele* or *syringo-myelocele*; in the third, the cord, it is supposed, is normally closed, but before it separates from the surface epiblast it becomes compressed by a collection of fluid within the meningeal spaces, *myelo-meningocele*; in the fourth, the cord is normal, but there is a local hernia of the membranes, *meningocele*; and in the fifth, the cord and membranes are normally formed, but the arches of one or more vertebræ are defective, although no protrusion of spinal contents takes place, *spina bifida occulta.*

Taruffi (84) has thought it necessary to conjoin with the theory of arrested development that of disease of the parts. In this he has followed Recklinghausen and others. Accordingly he ascribes the state of the cord and its membranes to the destructive effects of a sort of angiomatous process similar to that which he thinks has led to the changes in the brain in pseudencephalus (*q.v.*). The factors are a pathological development of the vessels along with exudations and hæmorrhages; and these, it is supposed, lead to destruction of certain parts of the cord and its membranes. It seems to me, however, that it is not necessary to bring forward this factor, for it is possible that the changes found may not be due to destruction of previously existing parts but to non-formation of them, or rather to imperfect differentiation of each one of them from the rest. Further, the vascular theory of Taruffi is only of use in explaining myelomeningoceles; it fails in the case of myelo-cystocele and of meningocele.

Cleland (7, 85), as has been stated already, favours the view of a reopening of the medullary canal from excessive collection of fluid within it in order to explain some varieties of spina bifida. He has also introduced (7) a new element into the teratogenesis of spina bifida and allied conditions by suggesting the factor of over-stimulation. He thus accounts for the osseous and cartilaginous projections which have been noted within the spinal canal; and the double state of the cord in some instances he ascribes to partial fission of the early embryo. The fission has not extended far, having resulted simply in the production of these "vestiges of duplicity," on the dorsum; but possibly (Cleland thinks) specimens of spina bifida may yet be discovered containing a trace of appended limbs.

I am of opinion that Cleland is right in introducing the idea of excess of development into the teratogenesis of spina bifida. I believe that the chief factor is arrested ontogenesis, and that the most of the structural peculiarities are its results, modified probably by the continued and unopposed growth and development of neighbouring parts and possibly also by pathological processes; but it seems to me that there coexists with this arrest of development a degree of excessive development, leading to the growth of cartilaginous and osseous projections from the vertebral bodies, to the presence of teratomata or teratoid neoplasms, and to the duplicity of the cord and its central canal (diastematomyelia). It is not uncommon to find this combination of defect and excess of ontogenesis in teratological specimens; and it is due, I believe, to what I have named the germinal factor in teratogenesis (p. 222). The tendency to excessive development is, I think, impressed upon the organism in the germinal or pre-embryonic epoch, and manifests its influence later. Perhaps O. Hertwig's experiments (*Arch. f. mikr. Anat.*, xxxix., 1892) on the production in frogs' eggs of malformations resembling spina bifida by means of polyspermy may be regarded as supporting this opinion. That there is sometimes a germinal factor in the production of spina bifida is a view which is also supported by the occurrence of several instances of the malformation in the same family (J. Burgh, 86; O. Zimmermann, 87; E. M. Pendleton, 88; P. Winge, 98; Mearns, 99; A. C. Butler-Smythe, 89), and in twins (Windle, 90). In considering this possibility, however, we must remember that we are forcing our way very far into the deepest mysteries of Nature's arcana, concerning which we must confess that our knowledge is but slight.

Treatment.

In the absence of any accurate knowledge as to the manner in which Nature attempts and sometimes successfully carries through the antenatal cure of a spina bifida, we have to think solely of postnatal reparative procedures. One thing, however, we may learn from Nature's works in utero—the necessity for asepsis. Whatever may be the process by which a defect in the spinal column is repaired before birth, we may be quite sure it is carried out aseptically. Now, since this book deals with Antenatal Hygiene it is not essential that I describe postnatal operative methods; so I shall simply refer to some of the plans that have been used and to them only in so far as a knowledge of the antenatal may throw light upon the postnatal.

It is doubtful whether tapping, compression, ligature, electrolysis, and simple incision of the spina bifida sac should be any longer countenanced by the surgeon or described in the text-books. None of these methods seems to me to be warranted by what is known of the morbid anatomy of the malformation. It is true that in a few cases cysts have been found in the neighbourhood of the spine and unconnected with its canal (Trowbridge, 91), and it has been thought that they represented spina bifida sacs shut off from the vertebræ in antenatal life by a natural process of compression or ligature; but these cysts are capable of being accounted for in other ways, and, even if they are the results of Nature's cure, we may be quite sure her methods had very little in common with such a crude method as ligature of the base of the sac. Even if a separation of the sac from the canal by a growth of the surrounding parts at its neck does occur, it must be supposed to be a very gradual process in no way resembling the sudden process of ligature; and, as has been already pointed out, it occurs in the aseptic medium of the uterine cavity. J. Morton (92), it is true, has obtained wonderfully good results (79·3 per cent. recoveries) from the combined method of tapping the sac (drawing off a portion of the fluid contents) and injecting the iodo-glycerine solution (10 grs. of iodine, half a drachm of iodide of potassium, and 1 oz. of glycerine) into the half-emptied cavity; but the operation most in favour at the present time would appear to be excision. Excision (described by Newbigging (95) in 1834) is not limited, as was at one time thought, to the meningoceles, but may be usefully employed in myelo-cystoceles and in many myelo-meningoceles. Of course in the case of myelo-meningoceles, the spinal cord and nerve roots must be preserved; if they are adherent to the sac they must be separated and returned to the canal, and if they are not detachable the cord must be put back with the part of the arachnoid to which it adheres. The attempt to bridge across the defect in the spinal canal by chiselling through and turning inwards the laminæ of the vertebræ or by bone grafting is unnecessary and, as H. J. Stiles (93) says, "only adds to the gravity of an already serious operation." In spina bifida occulta we find the opening in the canal closed by fibrous tissue, and there is often a pad of fat and connective tissue over it; in operative closure we ought to aim at the same result and bridge across the aperture with the edges of the sac and perhaps with periosteum, covering over the weak spot with two flaps taken from the erector spinal muscles and sutured together. In this way the opening can be closed and protected after closure by a sort of natural truss.

The coexistence of hydrocephalus is a contraindication to operation, as is also the presence of complete paralysis of the lower part of the body and the association of the spina bifida with grave malformations in other regions. Large size is not necessarily a contraindication, for it is remarkable to what an extent skin can be drawn from surrounding parts to supply the deficiency. The most serious impediment to success is the unsuspected presence of hydrocephalus; for I have shown how this may be found after the death of the infant although it could not be diagnosed during life (*vide* Plate XVIII.). The operation need not be postponed much after the first month of life is past; it may, if necessary, be performed earlier (93). Spina bifida, therefore, is in some of its forms (*e.g.* the occult) not necessarily fatal to postnatal life, while in other forms it may be operated upon with a fair hope of ultimate success if hydrocephalus be not associated with it. The results of Stiles (93), Nicoll (94), and a great many other surgeons, both at home and abroad, are decidedly encouraging, especially when it is remembered that it is not so long ago since all operative interference was regarded as well-nigh hopeless. Reparative Surgery has done much and will do more for the correction of antenatal malformations.

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CHAPTER XVIII

Merosomatous Terata (*cont.*): Malformations of the Spine (*cont.*): Minor Types of Spinal Deformity; Spinal Curvature; Scoliosis; Cyphosis; Lordosis; Spinal Retroflexion; Spondylolisthesis; Numerical Anomalies in Vertebræ; Fusion of Neighbouring Vertebræ; Assimilation; Fœtus Anurus; "Tails"; Tailed Races; Sporadic Cases of Homo Caudatus; Spurious Tails; True Tails, Varieties, Complications, Teratogenesis; Sacral Dimples and Infundibula; Miscellaneous Malformations of the Spine; Malformations of the Spinal Cord (Double Central Canal; Heterotopia of White and Grey Matter; Hydromyelia and Syringomyelia).

Spina bifida may be regarded as the central or major type of all the malformations that affect the spine and its contents. For this reason I described it in some detail, giving, as it were, a full-length portrait of it; but there are minor types of spinal deformity, and they require only to be sketched in outline. Some of them, however, are interesting both from the theoretical and the practical standpoint, and each one of them suggests attractive problems in disorderly ontogenesis. Many of them may be met with in association with spina bifida; they may also, however, occur alone.

Spinal Curvature.

As has been shown in the two preceding chapters, spinal curvature of a marked kind is present in iniencephaly and spina bifida; it will be met with again when the consideration of anencephaly and exomphalos and sympodia is undertaken. In these monstrosities the spine may show cyphosis, lordosis, or scoliosis; the last-named deformity has rendered itself particularly prominent in my eyes when I have been engaged in the making of frozen sections of teratological specimens, for, on account of it, the middle line of the body was lost at one point or another in the section. But spinal curvature may exist in the fœtus apart from other malformations, and it is with that form that I have here to do. There can be no doubt that some of these cases are to be regarded as fœtal diseases; in other words, they arise in the fœtal period of antenatal life from such causes as muscular retraction or paralysis and a faulty or restrained attitude of the unborn infant (Perdu, *La Scoliose*, Paris, p. 18, 1902). On this subject Guérin's work (*Recherches sur les difformités congénitales*, Paris, 1880) may be consulted with profit. But there are also cases in which the spinal distortion would appear to be due to causes arising in the embryonic period. To this group belong the instances of scoliosis arising from defects in the vertebral bodies.

Congenital Scoliosis.

A. Mouchet (*Bull. Soc. anat. de Paris,* 6 s., i. 972, 1899) has reported three cases of congenital scoliosis due to vertebral anomalies; two of these were dead-born fœtuses showing numerous malformations (exencephaly, congenital amputations, facial anomalies), and do not at present concern us; the third was a living female child who showed no other deviations from the normal. In this last-named instance the spinal anomaly was discovered by the radiograph, and consisted in the presence of a supplementary half-vertebra between the first and second lumbar vertebral bodies on the left side. The half-vertebra was wedge-shaped, the base being to the left and the apex to the right. A similar case was reported by G. Sangiorgi (*Arch. di ortoped.*, xviii. 65, 1901). There is a specimen of congenital malformation of the spine in the Museum of the Royal College of Surgeons of England (*Catalogue of the Teratological Series*, p. 95, 1893), in which there is a sharp lateral curve in the dorsal region, apparently due to absence of the right half of the third dorsal vertebra; there are other malformations, such as the presence of only seven ribs on each side and osseous union of the left scapula to the spine. Noble Smith (*Clin. Sketches*, ii. 72, 1895) has referred to similar cases. Half-vertebræ have been observed by other observers and without the association of scoliosis; in such cases there may be a compensatory atrophy of the bodies of adjacent vertebræ, or there may be a second half-vertebra on the opposite side of the spine (Salaghi, *Arch. di ortoped.*, xvi. 172, 1899). Salaghi (*loc. cit.*, p. 86) has also recorded a case of congenital dorso-lumbar scoliosis on the right side, in which the whole of the left half of the body and head of the infant was unduly small and in which there was left-sided torticollis; the cause, in this instance, may have been amniotic compression. Perhaps the amniotic pressure may, in some cases, be the agent which produces the half-vertebra; but even if this be so, it seems necessary to suppose some local defect in the affected vertebra to explain why it in particular and not the whole spine should be influenced by the compression. Whatever may be its cause, congenital scoliosis is a rare affection, occurring, according to Coville (*Rev. d'orthop.*, vii. 301, 1896) only once in one thousand new-born infants. A recent case is that reported by H. Maass (*Ztschr. f. orthop. Chir.*, xi. 411, 1902–03). It would seem to occur also in the lower animals, for there are specimens of it in fish, in birds, and in a calf in the Museum of the Royal College of Surgeons of England (*op. cit.*, p. 94), and Gurlt (*Lehrbuch d. path. Anat. d. Haus-Säugethiere*, ii. 173, 1832) has described cases in the calf and the lamb under the name Campylorrhachis scoliosa.

Congenital Cyphosis and Cypho-Scoliosis.

Cyphosis of one or other region of the spine may be met with in association with spina bifida, anencephaly, exomphalos, and other anomalies; but it may also occur, in rare cases, practically alone, as in L. Bernhard's observation (*Arch. f. Kinderh.*, xxx. 31, 1900). In this case there was abnormally advanced ossification of some parts of the skeleton, and it was noted that attempts had been made to bring the pregnancy to a premature end. The cyphosis was in the upper dorsal region, and there was no compensatory lordosis. Cyphosis is usually conjoined with lordosis, the one curvature compensating the other; but the compensation is often incomplete. Instances of cyphotic scoliosis of antenatal origin in the lower animals have been recorded by Gurlt, Goubaux, Billiet, and Gotti (Taruffi, *Storia della teratologia*, vii. 135, 1894).

Lordosis, Spinal Retroflexion, Spondylolisthesis.

Antenatal *lordosis* and *spinal retroflexion* are generally combined with such grave types of monstrosity as exomphalos, iniencephaly, and anencephaly (*q.v.*); but Matthews Duncan (*Trans. Obstet. Soc. Lond.*, xxvi. 217, 1885) has described an interesting case in which none of these teratological states was present. It was that of a full-time male fœtus with a large (slightly hydrocephalic) head; the trunk was apparently normal, but the head and all the limbs were doubled backwards towards the spine, and fixed in their abnormal position by "amniotic" bands consisting of skin. Matthews Duncan believed the specimen to be unique, and I have met with no similar one in teratological literature; but a case resembling it in some points has been reported by C. B. Lockwood (*Trans. Obstet. Soc. Lond.*, xxix. 234, 1887). Lockwood's specimen was a fifty days old human embryo, showing a remarkable degree of retroflexion, but with no amniotic bands to account for it such as were found in Duncan's fœtus; it had no spinal cord, and the vertebral column was very short and without neural arches or spines; there was a notochord which was single in the upper cervical and dorsal regions, and double in the lower cervical. Lockwood thought that the cause of the retroflexion was to be found in the fact that the spinal column had failed to develop, while the viscera at its ventral surface had both developed and grown and forced the pelvis and lower spine dorsally. Whether Lockwood's explanation be correct or not, the observation is a most interesting one on account of the early period in antenatal life to which it is necessary to refer the production of the lordosis; it is evident that one is warranted in regarding some at least of the cases of congenital spinal curvature as embryonic in origin.

The Comparative Teratology of lordosis suggests some interesting reflections. It has been found that retroflexion of the spine is out of all proportion more frequent in the calf than in any other animal; in fact, with the exception of one case in a foal (Joly, *Mém. de l'Acad. d. sc. Toulouse*, i. 259, 1845), it would seem to be only met with in the calf. This is one of the most interesting lines along which research may yet travel in the solution of the problems of Teratology; for there must be some reason why one monstrosity specially affects one animal type rather than others. In the case of the calf the retroflexion of the spine is almost constantly associated with an open condition of the anterior (or *inferior*) thoracic and abdominal wall; more than this, the ribs are curiously turned backwards (or *upwards*) to form a sort of spurious thoraco-abdominal cavity above the dorsum. This new supradorsal cavity has, therefore, walls lined on the outside with a serous membrane and on the inside by skin; to the lordotic spine are attached the thoracic and abdominal viscera which hang downwards in two packets, as it were, with traces of the diaphragm separating them. On account of the open state of the thoraco-abdominal cavity, Gurlt (*Lehrbuch d. path. Anat., etc.*, ii. 137, 1832; *Ueber thierische Missgeburten*, p. 25, 1877) gave to this type the name *schistosomus reflexus*; while Joly (*Ann. d. sc. nat.*, 3 s., iii. 374, 1845), looking to the general turtle-like appearance of the monstrosity, called it *chelonisoma*. Dareste (*op. cit.*, pp. 418, 549, 1891) has given a good description of two specimens. Attached to the ends of the ribs which are turned backwards over the dorsum are parts of the divided sternum, and inside the new costal cavity are the scapulæ. Further, the head may be turned back and lost from view in the cavity; in other cases it is the tail and posterior extremities that thus pass from sight; the former arrangement would seem to be the rarer one. There may also be incomplete degrees of both displacements associated with rotation of the spine and resulting in the production of very curious and puzzling forms of monstrosity; and, finally, both the anterior and posterior limbs, the tail, and the head may be enclosed in the dorsal cavity, giving rise to an ovoid mass to which are attached the thoracic and abdominal viscera.

Spondylolisthesis may be considered along with lordosis, although it differs therefrom in certain particulars. It consists in a dislocation forwards and downwards (into the pelvic brim) of the body of the fifth lumbar vertebra, which, therefore, comes to lie more or less in front of the first sacral vertebra; it is, in consequence, a malformation which takes on great importance from the point of view of the obstetrician. F. Neugebauer (*Arch. f. Gynæk.*, xix. 441; xx. 133, 1882; xxi. 196, 1883; xxii. 347, 1884; xxv. 182, 1885; *Ann. de gynéc.*, xxi. 100, 1884) and many other writers have investigated the form of *pelvis obtecta* which is produced by the overhanging and displaced lumbar vertebra. The displacement probably occurs only in postnatal life; but in some cases at least it is made possible by an antenatal defect. Lambl (*Beitr. z. Geburtsh. u. Gynæk.*, iii. 1, 1858) regarded the defect as of the nature of a localised form of spina bifida, but Neugebauer thought it much more probable that it was due to an imperfect ossification and incomplete union of the interarticular parts of the vertebral arch of the fifth lumbar vertebra ("spondyloschizis interarticularis congenita arcus vertebralis"). Lambl (*Centr. f. Gynäk.*, ix. 356, 1885) made a strongly worded reply to Neugebauer's criticisms, and, on the whole, it seems to me to be quite possible that something of the nature of spina bifida might be the cause of the separation of the body of the vertebra from its arch. It may be mentioned here, as a curious addendum to the matter under discussion, that *steatopyga* is apparently due to or associated with a separation between the body of the last lumbar vertebra and the base of the sacrum (D. Lambl, *Centr. f. Gynäk.*, v. 256, 281, 1881), producing a backward tilting of the whole sacrum. Steatopyga, it will be remembered, is the name given to the accumulation of fat on the buttocks which is found in several African races, and especially in the women of the Hottentots or Bushmen. It is not clear whether the spondylolysis associated with steatopyga is a racial antenatal peculiarity or not; but investigations of an interesting nature seem to be possible in this direction. It is perhaps somewhat significant that a so-called *racial birth-mark* over the back in the region of the sacrum has been described (Matignon, *Arch. clin. de Bordeaux*, v. 416, 1896). It is said (Ashmead, *Sci-i-Kwai Med. Journ.*, xiv. No. 1, 1896) to be present in all Japanese babies as a dark blue spot which vanishes during the first two years of life; and it is believed to be present as early as the fifth month of fœtal life. The pigment is situated in the corium. This so-called racial birth-mark has been referred to by many recent authors. J. Deniker (*Bull. et mém. Soc. d'anthrop. de Paris,* 5 s., ii. 274, 1901), for instance, says it is not peculiar to the yellow races of mankind; it is found in Polynesia and among the Esquimaux. Although neither steatopyga nor this lumbo-sacral nævus can be regarded as peculiar to or constant in any one race, they nevertheless suggest two reflections: one of these is the tendency which some malformations have to affect one race rather than another; and the other is the frequency with which the lumbo-sacral region is the seat of anomalies of various kinds. From such racial and regional peculiarities it ought to be possible to learn something of the ultimate causes of monstrosities.

Numerical Anomalies in the Vertebræ.

An increase or a decrease either in the total number of vertebræ (33) or in the number of them in each region may occasionally occur. Numerical anomalies, like the malformations above referred to, seem to be commoner near the posterior (caudal) end of the spine; they are also commoner in the terminal members of the various series than in the middle ones. It is rare, therefore, to find either an increase or a decrease in the number of cervical vertebræ. There are, however, some cases of eight cervical vertebræ (Regalia, *Arch. per l'antrop.*, Firenze, x. 305, 1880; Dubreuil, *Gaz. méd. de Par.*, 3 s., iv. 871, 1849, etc.), although some doubt may exist whether the additional vertebra was a cervical one (with or without ribs) or a dorsal. Six cervical elements have also been noted (H. Coote, *Med. Times and Gaz.*, n.s., viii. 56, 1854), but diminution in the number would seem to be nearly always associated with such grave states as anencephaly and spina bifida. An additional dorsal vertebræ (making thirteen in all) may be found at the caudal end of the series; in such cases there may be twenty-six instead of twenty-four ribs. On the other hand, the twelfth dorsal vertebra, with its ribs, may be wanting (Tenchini, *Ateneo med. parmense,* i. 97, 1887; P. Topinard, *Rev. d'anthrop.*, vi. 577, 1877). Sometimes these numerical defects or excesses in one region would appear to be compensated by excesses or defects in another region of the vertebral column; but this is not constant. Variations in the number of the lumbar, sacral, and coccygeal vertebræ are comparatively common; they will be referred to later (p. 317). These numerical variations in the vertebræ must have their origin early in embryonic life, if we accept the theory that they are due to an original excess or deficiency in the number of the mesodermic somites and of the sclerotomes derived from them. Such anomalies may be expected to throw some light upon the metameric theory of the constitution of the body.

Fusion of Neighbouring Vertebræ, Assimilation, etc.

Several cases are on record of fusion of contiguous vertebræ. This process is normal in the sacral and coccygeal regions, and may on this account be termed sacralisation of the spine. It has been noted in the case of the atlas vertebra and the occiput by K. Bockshammer (*Diss. inaug.*, Tübingen, 1861), T. C. F. Serger (*Diss. inaug.*, Halle a. S., 1888), D. D. Slade (*Boston Med. and Surg. Journ.*, cxxxiii. 57, 1895), Mouchotte (*Bull. Soc. anat. de Paris*, s. 6, i. 873, 928, 1899), Regnault (*ibid.*, ii. 691, 1049, 1900), and Apert (*ibid.*, iii. 58, 1901); in the case of the odontoid process and the atlas by G. Romiti (*Boll. d. Soc. tra i. cult. d. sc. med. in Siena*, iv. 99, 1886); in the case of the axis and third cervical by Bancroft (*Proc. Acad. Nat. Sc. Phila.*, p. 419, 1891); and in that of the sixth and seventh cervical vertebræ by S. Bianchi (*Arch. per l'antrop.*, Firenze, xix. 93, 1889). Far more interesting, however, are the anomalous relations which may exist between the last lumbar and the first sacral vertebra or between the last sacral and the first coccygeal. Under normal circumstances the sacrum is formed by the union of the 25th, 26th, 27th, 28th, and 29th segments of the spinal column. Occasionally, however, it is made up of six segments, and the additional vertebra may be either the fifth lumbar (the 24th) or the first sacral (the 30th). Now there exists at various levels in the spine a tendency for the terminal members of one region to take on some of the characters of the members of the immediately adjacent region; these vertebræ may be described as showing assimilation. A good example is found in the presence of a foramen at the root of the transverse process of the first dorsal vertebra (W. Gruber, *Arch. f. path. Anat.*, lxvii. 341, 1876; W. Turner, *Journ. Anat. and Physiol.*, xvii. 255, 1882–83; xviii. 223, 1883–84); but a better is to be had in connection with the sacrum. Not only may the fifth lumbar (24th segment) resemble the first sacral in its characters, but it may also imitate it in its relation to the vertebra immediately following it, in other words it may fuse with it. This assimilation and fusion may be bilateral and complete or unilateral and imperfect, and in this way are produced two varieties of abnormal pelvis, that deformed symmetrically by assimilation of the fifth lumbar vertebra, and that deformed asymmetrically. In other cases it is the first coccygeal vertebra which takes on sacral characters and is fused with the fifth sacral; in this way another type of the pelvis deformed by assimilation is produced. The last-named arrangement differs from the simple anchylosis of the coccyx to the sacrum in the sacral characters assumed by the first coccygeal vertebra. E. Tridondani (*Ann. di ostet. e ginec.*, xxiv. 1–44, 1902) has written a very interesting article on these "pelves by assimilation" ("*bacini da assimilazione*"), in which he shows, among other things, that such deformed pelves often show other anomalies besides the fusion of the fifth lumbar and first sacral vertebræ: spina bifida, for instance, may coexist, as may also incomplete fusion of the sacral segments themselves, and traces of imperfect union of the pubic and ischial bones. Tridondani concludes that the sacral anomaly is not due to rickets but is an arrested development, and, from the fact that in the anthropoid apes the vertebra which forms the sacral promontory is variable, he thinks that atavism may possibly be invoked to explain the arrest in development.

Other abnormal fusions may take place in connection with the sacral vertebræ. The obliquely-contracted *pelvis of Nægele* is well known to obstetricians, and is generally regarded as due to a unilateral anchylosis of the sacrum and the ilium; according to some there is a premature ossification in the cartilages of the sacro-iliac articulation leading to the synostosis, and this may be due to a fœtal osteoarthritis; according to others there is an antenatal defect in the development of the lateral mass of the sacrum and of the adjacent ilium; and, according to yet others, the starting-point is unusual intrauterine pressure coming to bear upon the pelvis and flattening it, and the pressure may be due to absence of liquor amnii or to the existence of a malformation of the mother's uterus (uterus unicornis, etc.). In the *pelvis of Robert* both the sacral wings are absent, and there is bilateral sacro-iliac synostosis; it may be due to the same antenatal causes as produce the Nægele pelvis; at any rate, an instance of it has been met with in the fœtus at birth (O. Graf, *Ein Fall von angeborenem querverengtem Becken*, Zürich, 1864). In connection with the antenatal origin of the Robert pelvis it is interesting to note that F. Billitteri (*Arch. di ostet. e ginec.*, i. 421, 498, 1894) has recorded a case in which this pelvic deformity was found in two sisters (family prevalence).

In the two malformations just described (the Nægele and Robert pelvis) the sacral defect is in the alæ and lateral masses, but there are cases in which the sacral bodies themselves may be absent. When this is the case the coccyx also is wanting. As we shall see, when we come to study sympodia, sacral and coccygeal defects are so common as almost to constitute an integral part of the monstrosity; but they may also occur, although rarely, in cases which show no signs of fusion of the lower limbs. A. F. Hohl (*Zur Pathologie des Beckens*, p. 61, Leipzig, 1852), for instance, has described the case of a new-born infant in which the sacrum was represented only by two thin pieces of cartilage corresponding to the first two segments of the bone; and H. Litzmann (*Arch. f. Gynæk.*, xxv. 31, 1884–85) has put on record the case of an adult woman who died from peritonitis after her third confinement, and in whom the fifth lumbar vertebra was rudimentary, the sacrum was practically absent, and the coccyx was represented by a small nodule of cartilage. Litzmann's patient was a twin, and he thought the pressure of the co-twin in utero might have caused the defect at the posterior end of the spine. C. C. Werthheim (*Monatschr. f. Geburtsk. u. Frauenkr.*, ix. 127, 1857) has met with absence of both sacrum and coccyx in a new-born infant; and Bland-Sutton (*Introduction to General Pathology*, p. 85, 1886) tells of a prematurely born infant in whom all the vertebræ below the first lumbar were absent, and adds that the mother had fallen in the fifth month of gestation and probably fractured the back of the fœtus. Yet another specimen exists in the Anatomical Museum of Brussels; it was shown to Neugebauer by Professor Albrecht (*Arch. f. Gynæk.*, xxv. 223, 1885); and in it only the first and second segments of the sacrum were represented. Albrecht called it a pseudo-pithecoid pelvis, from its resemblance to what is found in the apes. O. Piering (*Ztschr. f. Heilk.*, x. 215, 1890) has recorded a case of short sacrum and apparent absence of the coccyx in an adult woman; there was an unusually long vulva with atresia ani vaginalis, the right scapula was situated at a higher level than usual, and some of the ribs were absent.

To the pelvis without a sacrum, Taruffi (*Storia della teratologia*, vii. 544, 1894) gave the name *acocono-lecanus*; he described instances of it in the calf and the pig; but he does not seem to have been acquainted with any instances in the human subject. In Comparative Teratology the term *perosomus elumbis* has been assigned by Gurlt (*Lehrbuch*, ii. 88, 1832). The description of these specimens of excess or defect of the sacral vertebræ naturally leads me to the consideration of the tailed and tailless fœtuses; but to them special paragraphs must be given.

Fœtus Anurus.

Since the human fœtus is normally tailless in the ordinary sense of the word it is hardly correct to speak of an anourous type of malformation in connection with it. At the same time the human embryo in an early stage of its existence is distinctly "tailed," and the remnant of that tail is found in the coccygeal vertebræ; so that it is not inappropriate to regard absence of the coccyx as equivalent to absence of the tail. The human coccyx is generally looked upon as a part in process of suppression; it is disappearing from the race. It is common to find numerical variations in such parts, and in this respect the coccyx forms no exception to the rule. The normal number of segments is four; but Calori (*Mem. d. r. Accad. d. sc. di Bologna*, s. 4, viii. 181, 1887) found five segments in 16 per cent. of the cases examined by him, and Staderini (*Monitore Zool. ital.*, v. 56, 95, 1894) put the percentage as high as 23. The latter writer met with three coccygeal vertebræ in 17 per cent. of the spines examined by him. Within normal limits, therefore, the number of the coccygeal vertebræ may be said to range from five to three. In the early embryo the number is probably always greater. When, therefore, the coccyx in the human subject is absent, either alone or in conjunction with some of the sacral vertebræ, it is not incorrect to speak of the fœtus as anourous or tailless. I. Newton Snively (*Med. News*, lxv. 545, 1894), for instance, has reported the case of a new-born male infant with several deformities, including absence of the coccyx and backward displacement of the lower end of the sacrum. Probably, if the fœtus anurus were more carefully looked for it would be more often noted.

As might be expected, absence of the tail is more commonly observed in the lower animals. The caudal defect may be either a shortening or an entire absence. It has been observed in a number of mammals, including the calf, sheep, pig, horse, cat, dog (Taruffi, *Storia della teratologia*, vii. 563, 1894), mouse (*Catalogue of the Teratological Series, etc.*, p. 80, London, 1893), and rabbit (*ibid.*, p. 120); but it may also occur in other types, *e.g.* in the sole among fish (*ibid.*, p. 120). In some of the recorded cases the coexisting malformations (*e.g.* anencephaly, existence of a cloaca, etc.) were so severe as to dwarf the importance of the anourous state. Gurlt (*Lehrbuch*, ii. 94, 1832) gave to the uncomplicated form the name *perocormus ecaudatus*; when it was associated with absence of the anus and cloacal formation, he called it *atretocormus aproetus*; and when it was combined with anencephaly and rhachischisis, Joly (*Gaz. d. hôp.*, Ann. xxviii. 191, 1855) described it as *anencephalus anurus*. The tailless state may occur sporadically: the anourous animal is the offspring of those that possess tails, and some curious family histories have been recorded. Mazzarelli (quoted by Taruffi, *op. cit.*, vii. 565, 1894), for instance, writes of a tailed male cat which impregnated two females which had both previously had normal kittens; on this occasion the kittens of both mothers had much shortened tails along with other abnormalities. Apparently, however, absence of the tail may become the character of a race, as in the famous cats of the Isle of Man and of Japan; the name *anurus endemicus* has been given to this racial type. In these animals the tail is not, as a rule, entirely absent, but it is reduced to five or six instead of twenty-two or twenty-three caudal vertebræ, and these are often somewhat twisted or fused together. Some interesting observations have been made on the results obtained when such tailless cats have progeny by the ordinary tailed variety. R. Anthony (*Bull. Soc. d'anthrop. de Paris*, 4 s., x. 303, 1899), for instance, has analysed the litters of kittens which a female Manx cat had by ordinary cats; among the twenty-four kittens (in six litters) there were ten that had long tails (like the father) and fourteen that had short ones like the mother, or none at all, or short ones although not so short as the mother's. The proportions in the various litters differed; thus, in one litter, there were five kittens resembling the mother and one resembling the father, whilst in another the paternal influence was seen in three and the maternal in one. Anthony concludes that the anourous state of the Manx cats is an anatomical character acquired long ago and so well fixed as to constitute a race. Whether, however, the originator of this tailless race was a sporadic case or the result of an accidental mutilation is not, of course, known. Here the individual case widens out suddenly into the large question of the heredity of acquired conditions. Into the fierce and prolonged discussion that has taken place round this disputed matter I cannot here enter, for it is rather a question of germinal than of embryonic pathology; but it may be said that there is, to my mind, some evidence, although it is neither large nor conclusive, that animals which have had their tails removed artificially do occasionally have short-tailed individuals in their progeny (R. Bonnet, *Beitr. z. path. Anat. u. allg. Path.*, iv. 67, 1888–89). Whether, however, they have them more frequently than can be accounted for by the occurrence of the usual sporadic cases is not clearly established. (A summary of recent views on this subject will be found in Delage's *L'Hérédité*, 2nd ed., pp. 222–226, 288, 297, 849, 1903.) With regard to the mode of origin of the sporadic cases, several theories have been advanced, but they are not altogether satisfactory: perhaps in some cases the mother animal bites off the tails of her offspring at birth, either intentionally or by accident (mistaking the tail for the umbilical cord); perhaps in other cases there is a paternal influence acting in some mysterious manner, as Mazzarelli's case suggests; and there are other hypotheses.

"Tails."

Not Teratology only but Anthropology and Ethnology are all concerned in the discussions which have taken place regarding the occurrence of "tailed infants"; *homo caudatus* or *uro-anthropos* (Taruffi) has always excited curiosity and aroused controversy. In Mythology, also, the records of tailed individuals and races are not wanting.

A great deal has been written and more has been rumoured about the existence of a tailed race of human beings. From the earliest times of Herodotus and Pliny and Ctesias, up to the most recent reports of modern African explorers, the credulous public has been asked to believe in the presence somewhere on the earth's surface of men with tails. Rumour has been busy with reports as to the geographical location of this tailed race: now, on an old map, we find it in Tierra del Fuego, the abrupt and laconic legend being "homines caudati hic"; again, it is in Polynesia (in New Britain), and the infants that are born without the caudal appendage are, so we are told, summarily killed; again, it is near the sources of the Amazon ("cependant je laisse à chacun ajouter la foi qu'il voudra à ces faits," adds a critical reporter), or in Trebizond in Asiatic Turkey among the descendants of Constantine the Great ("d'ailleurs la puissance de Dieu est infinie; il fait tout ce qu'il lui plait, et crée, quand il le veut, des objets inconnus aux hommes"), or in Turkestan ("stinkendes Ungeziefer mit Schwänzen"), or in India in Rajputana ("the long-tailed Ranas of Saurashtra"), or in China, or in Japan, or in Formosa, or in the Malay peninsula, and the islands of Borneo, Sumatra, and the Philippines; but in Africa more perhaps than in any other part of the world have there been reiterated "travellers' tales about tails" (in Marocco, among the Niam-Niams of Central Africa, in Loango, in Bornu, etc.). Even in Europe, more especially in the west and south, there are legends, usually of considerable antiquity, of the occurrence of tailed peoples. Scotland and England are not without their records; and the people of Rochester ("illa gens incredula") seem to have been most unfortunate, for by offending first St. Augustine and later Thomas à Becket, their children were born with tails, as a mark, so the chroniclers say, of God's displeasure. The reader who may desire to know more concerning these quaint beliefs of the past will find what he wants in Bartels' classical papers (*Arch. f. Anthrop.*, xiii. 1, 1881; xv. 45, 1884) and in the many references which they contain. Some articles which have appeared in recent years and which may also be consulted are by Tirant (*Bull. Soc. d'anthrop. de Lyon*, i. 158, 1881–82; ii. 157, 1883), J. Wilson (*Ztschr. f. Ethnol.*, xii. 74, 1880), T. H. Parke (*My Personal Experiences in Tropical Africa*, p. 397, 1891), P. D'Enjoy (*Anthropologie*, vii. 531, 1896), and Zaborowski (*Bull. Soc. d'anthrop. de Paris*, 4 s., viii. 28, 1897).

Some parts of the evidence regarding the tailed races have been hearsay, and, therefore, outside the province of scientific inquiry; and other parts of it have been founded upon observations upon tailed individuals made at such a distance as to leave the possibility that the caudal appendages were of the nature of attached ornaments and were not structurally united to the body. The tailed peoples have always shown a tendency to recede as the curious traveller or anthropologist advanced towards them, and when he reached his furthest point it was to find that the "homines caudati" were still three or four days' journey further on. There is no really reliable evidence of a tailed race of human beings, although, as we shall see immediately, there are not a few records of individuals with tails or with caudal appendages resembling tails. "Homines caudati hic" cannot yet be written over any part of the world's surface; but it is more than likely that in every country a tailed baby now and again makes its appearance, to cause loud wonder among the vulgar and suppressed scientific excitement among the learned.

Let us look now at the individual or sporadic cases of caudal appendage which have been put on record at various times and in various places. Some of the older records contain in them a suggestion of the mythical, although the illustrations that accompany them are apparently most convincing. As a type of such ancient and dubious cases I may cite that reported by Krahe (*Phil. Trans.*, xiv. 599, Oxford, 1684). It is entitled "The Description of a Monstrous Child, born Friday, the 29th of February 1684, at a village called Heisagger, distant about four English miles from Hattersleben, a Town in South Jutland, under the King of Denmark's Dominion, communicated by Mr. Christopher Krahe, a member of the Ecclesiastical Consistory and Provost of all the Churches belonging to the said Diocess." The record, then, is most circumstantial, and the reader who doubts may find Hattersleben (or Hadersleben) on the map, in South Jutland, just as is affirmed. The mother of the child was wife of a soldier; the infant's legs looked as if they had been hacked, and there were swellings on them like bullets; and a maternal impression is therefore indicated. "The face did look pretty old"; and at the forehead there were excrescences, "as if it were artificial laces." "With the left eye it did look fiercely, keeping that other close." There were also malformations of the back of the head, of the left arm, and of the toes. The description of the tail (which is shown almost reaching the ground in the figure) is disappointingly short: "the Tail, which was strangely grown out of the back-part, was a quarter of a Sealandish Ell long." The mother had two other sons, alive and well; "but this Monster, after it had cryed out 2 or 3 times, died presently." The tail, long and thin, is represented as springing from between the buttocks just above the anus. It is difficult to know what to make of this record: but the most probable explanation is that an infant deformed in a way resembling the description given was actually born and died where and when it is stated; and that the artist considerably lengthened the tail, and tried to give some touches of artistic verisimilitude to the lower limbs in accordance with the father's military experiences. A suspicion of the same æsthetic amplification attaches to the illustration which accompanies J. S. Elshott's description of a "Puella monstrosa," who had an umbilical hernia, a left arm ending in a point, deformed digits, and two rat-tail-like appendages, one attached to the right thigh and the other over the tip of the coccyx. By a curious coincidence, the father of this infant was also a soldier (*Miscel. Acad. nat. curios.*, iv.–v., Append. p. 80, 1676). I need cite no others of these seventeenth century cases, for the two already mentioned will serve as types. It is to be regretted that the shadow of doubt rests upon them, for if they were free from it they would stand out prominently as the best instances that we possess of truly tail-like tails in the human subject. The shadow, however, does rest upon them.

Before I proceed to describe some modern examples of tailed infants, it may be well worth while to narrow down the whole subject by excluding the "false tails." In the first place, it is necessary to set aside sacro-coccygeal neoplasms of all kinds. I recently saw (with Mr. Stiles) a female infant with a large tumour attached to the post-anal region which, when examined by the Röntgen rays, was found to contain a spinal column and ribs; obviously this was not a tail but an attached twin or parasitic fœtus. Teratomata, teratoid growths, and dermoid cysts may also grow in this region; Thirk's case (*Oesterr. med. Wchnschr.*, N. 36, 1121, 1847) and Jacob's (*Dublin Hosp. Rep.*, iv. 571, 1827) probably both belong to this group. Lipomata, also, of the sacral region are not tails, although when they become pendulous, as in one of Bartels' cases (*Deutsche Ztschr. f. Chir.*, xx. 100, 1884) and in Fieux' case (*Rev. mens. de gynéc. d'obst. et paed. de Bordeaux*, iv. 456, 1902), they may closely simulate them. All caudal appendages composed of fat are not, however, of necessity lipomata, for Virchow found in one of them (Greve's specimen) some traces of the notochord (*Arch. f. path. Anat.*, lxxii. 129, 1878; lxxix. 176, 1880). Again, the sac of a spina bifida of the sacral region must not be mistaken for a tail (Fig. 54); at the same time a caudal appendage and a spina bifida sac may be associated, as we shall see immediately Neither can we regard the hairs which sometimes arise over a spina bifida occulta, and grow to some length, as a true tail. These various structures may all become caudiform, but they are to be separated off from human tails.

I have personally been able to examine several cases of "tails" and "pseudo-tails." In one of these (Fig. 51) there was an open lumbar spina bifida, and below it a thick caudiform growth with a little button-like projection at its lowest point; it seemed to be no more than a lipoma. In another case (Fig. 29) there was a sacral spina bifida sac; and in another (Fig. 31) there was a conical projection which seemed to contain the lower end of the spinal column, and from the tip of which an amniotic band took origin. The latter of these two cases has some claim to be regarded as a tail. In another case, which I saw in January 1902, there was a curious combination of spina bifida and tail: the child, a male, was fifteen months old when brought under my notice by Dr. T. J. Thyne; it was born six months after the death (from typhoid fever) of the father, and the mother had one other child, a female, nine years of age, and normally formed; the infant had a sacral spina bifida sac, covered with skin, and measuring 6 inches in circumference, and from the apex of this there projected a tail-like appendage. The "tail" was 1 inch in length, and was covered with normal skin; it was quite soft; it consisted of two parts, a proximal, resembling the first phalanx of the little finger, and a much thinner distal part, more tail-like. Unfortunately, a photograph of this caudal appendage was not obtained. It had resemblances to that described some time ago by Edmund Owen (*Trans. Path. Soc. Lond.*, xxxix. 425, 1888), who compared it to a "fat little finger." In yet another case which came under my notice there was a "tail." This was the fœtus, appearing in Figs. 48 and 49 in vol. i. of this MANUAL (p. 341); it suffered from an exuberant overgrowth of cartilage in various parts of the skeleton (*chondrodystrophia fœtalis hyperplastica*), and the coccyx, participating in this change, grew into a marked "tail."

What may be called "true tails" may be subdivided into those which contain bone or cartilage and those which do not (soft tails), or into those which are attached or adherent ("die angewachsenen Schwänze," Bartels) and those which are free ("die freien Schwänze," Bartels). Of tails containing bone or cartilage or rudiments of vertebræ there are very few specimens known. T. Bartholin (*Hist. anat. et med. rar.*, cent. vi., hist. 44, p. 268, 1681) and M. F. Lochner (*Miscel. Acad. nat. cur.*, Dec. ii., Ann. vii. p. 230, 1689) have recorded cases in which it is stated that more than five coccygeal vertebræ were present in the tail; but it is a pity that the details are not more convincingly stated, and that Lochner writes "in a merry vein," as Jacob (*loc. cit.*) puts it. No modern instance has been reported of a human tail containing more than the usual number of coccygeal vertebræ, namely, three to five, and even of them there are very few (Voltaire, *Dict. philos.*, xi. 211, 1832; Ornstein, *Ztschr. f. Ethnol.*,

xi. 303, 1879; C. Hennig and A. Rauber, *Arch. f. path. Anat.*, cv. 83, 1886). Of specimens containing cartilage or rudiments of the notochord I may refer to those of J. Wilson (*Ztschr. f. Ethnol.*, xii. 74, 1880), of S. Blancard (*Collectanea medico-physica*, Amsterdam, 1680–88), of Fleischmann (1841) and Gerlach (*Morphol. Jahrb.*, vi. 106, 1880), and of J. H. F. Kohlbrugge (*Natuurk. Tijdschr. v. Nederl. Indië*, lvii. 163, 1898). As an example of this group of tails, I may cite the case described by Hennig and Rauber (*loc. cit.*, *supra*).

The mother of the tailed infant seen by Hennig was a I-para; she was a dairymaid, and had got a fright at the parturition of a cow. Her child, a female, presented by the breech, and there was very little liquor amnii; it was only 29 cms. in length, the lower limbs being short. The upper part of the body was well formed, and the number of vertebræ above the sacrum was normal. The lower limbs showed several malformations (peromely), and there was átresia ani vestibularis and absence of the labia majora. There was a post-anal dimple (*foveola coccygea*) 1 inch above the base of the tail; it corresponded to the apex of the sacrum, and it was surrounded by a ring of hairs. The sacral vertebræ were only four in number. There was a groove from the post-anal dimple to the root of the tail. The tail itself was a little over an inch in length (2·7 cms.), was somewhat triangular in form, was covered with normal skin, had some lanugo hairs at the tip, and possessed a hard core. The core consisted of cartilage, made up of a proximal and a distal part, apparently representing five vertebræ. The tail was somewhat flattened at the tip, and contained, in addition to the cartilage, some muscular fibres (levator caudæ or extensor coccygis, etc.). On more minute examination the two segments of the tail were found each to consist of a small cylinder of bone (diaphysis), with two extremities (epiphyses) of hyaline cartilage; they may be regarded either as vertebræ arrested in development, or as a parasitic appendage, but the authors regard the former as the more probable conclusion. They were attached by a fibrous band to the sacrum.

Of soft tails several specimens have been reported. They may be attached or free: of the former I may mention Labourdette's case (*Journ. gén. de méd., chir., et pharm.*, xxxii. 375, 1808), and those of Bartels (*Arch. f. Anthrop.*, xiii. 1, 411, 1881) and of H. W. Freund (*Arch. f. path. Anat.*, civ. 531, 1886); and of the latter, those of Oskar Schæffer (*Arch. f. Anthrop.*, xx. 189, 1891–92), of Pyatnitski (*Diss. inaug.*, St. Petersb., 1892), of K. N. Vinogradoff (*Vrach*, xv. 901, 1894), of W. Scheboldaeff (*Zemsk. Vrach*, vi. 2, 28, 1893), of R. G. Harrison (*Johns Hopkins Hosp. Bull.*, xii. 96, 1901), and of E. Hagenbach (*Arch. f. klin. Chir.*, lxvi. 426, 1902). The attached tail usually consists of a triangular elevation of the skin covering the lower end of the sacrum; it passes to one side of the anus and may become continuous with the raphé in front of it. Harrison's example of a free soft tail is a typical one, and calls for a brief description.

In the case exhibited in 1900 by Watson (*Johns Hopkins Hosp. Bull.*, xi. 114, 1900) and examined by Harrison (*ibid.*, xii. 96, 1901), the tail was attached to a male infant, who showed no other anomaly save shortening of the toes of one foot (two phalanges in each). The tail (Fig. 55), which was 1¾ inch long at three weeks and 2¼ inches at three months, arose about ½ inch below the coccyx. Above its root was a groove leading to a well-marked post-anal dimple (foveola coccygea). It was covered with normal skin, had a firm but not a hard consistence, and it had three recognisable segments. The basal segment was short and was evident only on the ventral side; the middle part was an inch in length, and was clearly separated by a constriction from the end segment; the last-named portion was curved to the right and ventrally, and ended in a rounded blunt extremity. There were numerous hairs, especially near the tip. It is very noteworthy that the tail was slightly movable: when at rest it lay extended in the middle line, but, when the child was irritated, it was contracted and the terminal segment was drawn in and flexed to the left side. After the tail had been amputated it was carefully examined. The skin was normal save on the ventral aspect, where there was some thickening of the epidermis. The sebaceous and sudoriparous glands were normal, and the hairs were obliquely inserted pointing towards the tip. The bulk of the tail was made up of areolar tissue containing much fat. There was no trace of notochord or spinal cord; but there were some bundles of voluntary muscular fibres which took origin from the subcutaneous tissue near the proximal end of the middle segment, and were inserted into the skin of the terminal segment mostly on its left side. No muscles passed from the trunk to the tail. There were several arteries and some small veins, also a number of small nerve trunks.

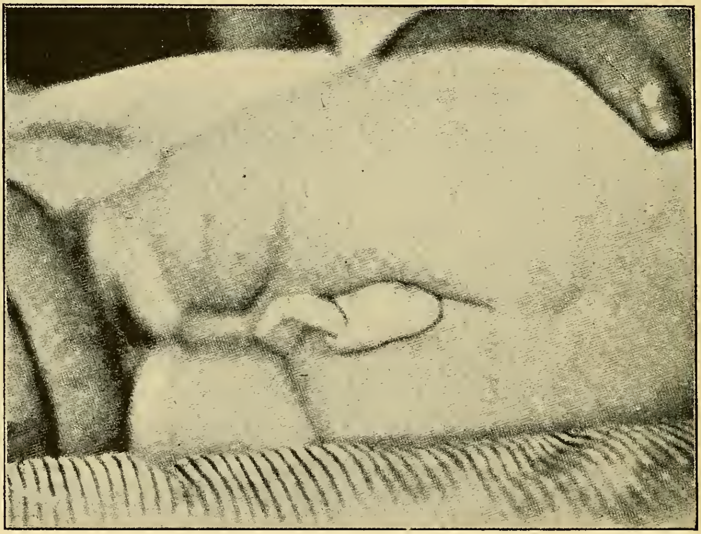

Fig. 55.—Harrison's Patient with Soft Tail.

Before I refer to the mode of production of tails I may take note of the fact that such structures are usually found in fœtuses which show other malformations. Schæffer (*loc. cit.*) has made a careful analysis of the associated malformations: among them were atresia ani, exomphalos, exstrophy of the bladder, asymmetrical development of the whole body, defective limbs, anomalies of the genital organs (*e.g.* hypospadias), amniotic bands, anencephalus, hypertrichosis, polymastia, and club-feet. A tail has also been found in double terata (Hohlfeld, *Diss. inaug.*, Würzburg, 1861; Becker, *Diss. inaug.*, Göttingen, 1889) and in several instances of sympodia. Its association with fusion of the lower limbs (sympodia) is particularly interesting: when it occurs it would seem that in some instances (*e.g.* Ruge's case, *Arch. f. path. Anat.*, cxxix. 381, 1892) the "tail" is due to a dislocation of the lower end of the spine backwards and to one side (as in one of my cases, Fig. 56); while in others it is simply a soft caudiform structure which is met with ("penis-like" in W. Maclaren's specimen, *Edinb. Med. Journ.*, xviii. 658, 1873; xix. 590, 1874; "soft, vascular, spongy, and obtuse" in J. Hofer's, *Acta Helvet.*, iii. 366, 1758; like a pig's tail in D. Superville's, *Phil. Trans.*, xli. 302, London, 1744; and with its tip of livid colour and divided into two lobules in B. W. Huesker's case, *Diss. inaug.*, Gryphiæ, 1841).

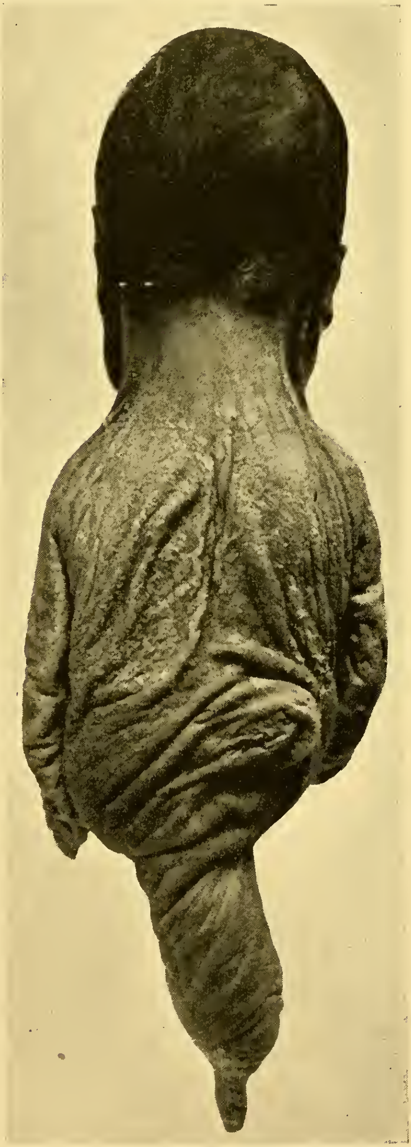

Fig. 56.—External Appearances, posterior view, of Uromelic (Sympodial) Fœtus with Caudal Projection. Specimen No. 250.

It is necessary, now, to consider very briefly what explanation Teratology has to offer for the occurrence of such true "tails" as have been described. Embryology supplies part of the answer, and the general principles of Teratogenesis when applied to this part of ontogenesis complete the solution of the problem. There is a stage in the development of the human embryo when it possesses a real tail; it is best marked in embryos of about 14 mms. in length (fifth week); and it may be well seen in Figs. 12, 13, and 14, and especially well in Fig. 17 (p. 54). Harrison's description of the tail in the human embryo (founded on the examination of Mall's specimens) is good, and I quote from it here. There are seven coccygeal vertebræ in embryos 14 mms. long, and from the third of these onwards is the "tail," *i.e.* the part which projects free from the trunk. Half of the length of the projection is occupied by the vertebræ, while the distal part contains no vertebræ; the former part may be called the coccygeal projection (*Steisshöcker*), and the latter the "caudal filament." The caudal filament is bent towards the dorsum and ends in a slight knob; the medullary cord (spinal cord) runs to the tip of it and ends in a vesicular swelling; the notochord and the terminal branches of the aorta (middle sacral) and inferior vena cava also pass into it, but not to the same distance as the medullary cord; and there is a mesenchymatous network in it with a thickened area, perhaps representing the post-anal gut of earlier embryonic life. At the level of the thirty-second vertebra (just above the base of the tail) the medullary cord suddenly becomes constricted to form the filum terminale; there are few or no neuroblasts beyond this point; and the walls are composed of columnar epithelial cells. As embryonic life goes on the caudal filament atrophies; the part containing vertebræ (coccygeal projection or *Steisshöcker*) remains for a time as a prominence, but gradually disappears by the growth and alterations in surrounding parts and by the reduction (by fusion) of the seven or six coccygeal vertebræ to five, four, or three. It begins, now, to be clear that these human "tails" are the result of arrested development. The soft, boneless tails are due to persistence of the caudal filament (His), and the rarer cartilaginous or osseous tails are due to the arrest of development in the later stage, when only the *Steisshöcker* is left. We are not in a position to explain completely how the arrest is brought about, or how the development of neighbouring parts affects it or is affected by it; but we may surmise, with Schæffer (*loc. cit.*) and others, that either amniotic compression or amniotic adhesions or both have something to do with it. It is interesting to note that several of the associated malformations (*e.g.* sympodia) are ascribed to amniotic narrowness, and it is quite possible that the caudal fold or part of the amnion may remain attached to the caudal filament or *Steisshöcker* and prevent its normal atrophy or its embedment in the surrounding structures. Human "tails," therefore, would seem to be due to the persistence of a state which is transitorily present in the human embryo itself; no evidence can be extracted from them to support the view that they are atavistic revivals of the animal tail of a far-back ancestor. Whatever may be its origin, the human "tail" had best be removed by the surgeon's knife to relieve the patient from its "discomfort and reproach."

Literature.—In addition to the references on "Tails" already given, I may add some others which have appeared, most of them subsequent to Bartels' articles in 1881 and 1884. O. T. J. Mohnike, *Uber geschwänzte Menschen*, Münster, 1878; Albrecht, *Ber. ü. d. Verhandl. d. deutsch. Gesellsch. f. Chir.*, p. 58, 1885; A. Ecker, *Arch. f. Anthrop.*, xii. 129, 1880; xiii. 483, 1881; Lissner, *Arch. f. path. Anat.*, xcix. 191, 1885; E. Sonnenburg, *Berlin. klin. Wchnschr.*, xxi. 790, 1884; H. W. Eaton, *Science*, iii. 673, 1884; A. V. Elissejeff, *Vrach*, vii. 295, 1886; H. E. Steinbach, *Diss. inaug.*, Berlin, 1889; Ch. Féré, *Nouv. iconogr. de la Salpêt.*, iii. 45, 1890; F. Keibel, *Anat. Anz.*, vi. 170, 1891; *Arch. f. Anat. u. Entwcklngsgesch.*, 356, 1891; K. A. Belinovski, *Chir. Laitop.*, ii. 57, 1892; Dickinson, *Brooklyn Med. Journ.*, viii. 568, 1894; J. Berry, *Memphis Med. Month.*, xiv. 105, 1894; V. N. Kniazeff, *Vrach*, xv. 903, 1894; C. Garcia, *Med. contemp.*, Lisbon, xv. 93, 1897; Unger u. Brugsch, *Ztschr. f. Ethnol.*, xxxv. 469, 1903; B. Chatterton, *Indian Med. Gaz.*, xxxviii. 300, 1903; Hennig, *Deutsche med. Wchnschr.*, xxix., *Ver.-Beil.*, 101, 1903.

Coccygeal Foveolæ, Infundibula, and Fistulæ.

What Max Bartels did for the study of "tails," Ecker may be said to have accomplished for the curious minor malformation known as the post-anal dimple or foveola coccygea (*Arch. f. Anthrop.*, xi. 281, 1879; xii. 129, 1880). The little depression or fossa situated behind the anus (which occasionally draws to itself the surgeon's attention by becoming a sinus, a fistula, or a cyst) had indeed been recognised before Ecker's time; but after his articles had made their appearance it was realised that a new teratological type had been added to the already long list, and that it had come to us along with an adequate embryological explanation of its mode of origin and meaning. Of contributions prior to the appearance of Ecker's papers I select two for brief note. One of these was by Lawson Tait (*Nature*, xviii. 481, 1878; *Rep. Brit. Ass. Adv. Sc.*, xlviii. 606, 1879): he found a well-marked sacral dimple or cutaneous depression over the lower end of the sacrum in 23 per cent. of the patients in the Birmingham Hospital for Women; he thought it indicated a cicatrix; and, from an observation on a tailless kitten, he suggested, somewhat fancifully, that it might be the hereditary cicatrix of the spina bifida by which the human tail had been lost. In the same year, Féré (*Bull. Soc. anat. de Paris*, 4 s., iii. 309, 532, 1878) described an infundibuliform circular depression at the level of the lower part of the sacrum in a child with a double uterus and vagina; he also met with a case in which the posterior surface of the sacrum-coccyx was vertical, while the point of the coccyx was turned backwards and had the infundibulum or dimple just over its tip, the skin being adherent to it by fibrous bands. He saw several other instances, and pointed out how cysts might form in them by retention of products from the glands of the skin. He regarded them as due to imperfect closure of the "posterior umbilicus," a somewhat hypothetical aperture.

Ecker's contributions to the subject (*loc. cit.*) contain also an investigation into the anatomy of the posterior end of the trunk in embryonic and in early fœtal life. He found in the case of the young fœtus and new-born infant that the lanugo hairs converge to form a vertex or vortex over the coccyx; this he called the vertex coccygeus (*Steisshaarwirbel*). Above the vertex was a small hairless area, the glabella coccygea; and in its neighbourhood there was sometimes a distinct depression or hollow, the foramen cæcum retro-anale (Hyrtl) or foveola retro-analis (Luschka). Ecker preferred to call the depression the foveola coccygea (*Steissbeingrübchen*). He found it in the fœtus, in the new-born infant, and even in adults, and sometimes it occurred in combination with a "tail." It usually was single and occupied the exact middle line, very nearly over the tip of the coccyx and at least 1 cm. behind the anal aperture; but it might be double and asymmetrical. It was not restricted to the fœtuses of European races, but occurred also among the Chinese and Mulattos.

In 1882, Terrillon (*Rev. de chir.* ii. 269, 1882) pointed out the association of the foveola with fistulæ, sinuses, and abscesses over the sacrum in the adult, and recorded three instances of inflammatory swellings in the intergluteal fold having this congenital origin. Reclus (*ibid.*, p. 342) described an instance of fistula arising from such a foveola, and Lannelongue (*ibid.*) spoke of a case in which a clinical thermometer was by mistake placed in such a depression instead of in the anus. The latter writer found foveolæ in 95 cases out of 130, while Heurtaux (*ibid.*, p. 343) met with 42 in 960, or 1 case in 23. A. Dunlop (*Lancet*, i. for 1882, p. 729) described several interesting instances of sacral dimple; he showed how in some cases it occurred in association with a coccyx which had a vertical direction or was turned back at the tip, while in others the coccyx was quite normal. Peyramaure-Duverdier (*Thèse*, Paris, 1882), J. Couraud (*Thèse*, Paris, 1883), H. Wendelstadt (*Diss. inaug.*, Bonn, 1885), and O. Madelung (*Centrlbl. f. Chir.*, xii. 761, 1885) also made contributions to our knowledge of this foveola or para-coccygeal infundibulum. F. Tourneux and G. Herrmann (*Journ. de l'anat. et physiol.*, xxiii. 498, 1887) tried to find a more satisfactory explanation of its origin: they showed that at first the medullary canal reaches the tip of the coccyx, where it becomes adherent to the deeper layers of the derma; then through the quicker growth of the spinal column the medullary canal (spinal cord) ascends; but coccygeal remnants ("vestiges coccygiens") remain uniting the coccyx to the skin and constituting the "caudal ligament"; about the sixth month of intrauterine life these remnants atrophy, the surrounding soft parts grow, the coccygeal projection is effaced by the straightening of the spine, and so the skin is drawn in as a dimple, foveola, or infundibulum. W. Zoege von Manteuffel (*Deutsche med. Wchnschr.*, xvi. 473, 1890) described two cases in which fistulæ resulted from inflammation in the foveolæ, and T. Wette (*Arch. f. klin. Chir.*, xlvii. 343, 1894) recorded seven instances of abscess and fistulæ, pointing out also the possible relation of the foveola to dermoid sacro-coccygeal cysts.

Féré (*Nouv. iconogr. de la Salpêt.*, x. 195, 1897) has in recent years drawn an interesting analogy between the hair vortex over the sacrum and that which exists over the cranium. He thinks they represent the posterior and anterior ends of the dorsal groove of embryonic life; each is, therefore, of the nature of an umbilicus, the posterior dorsal and anterior dorsal umbilicus. Anomalies may occur in connection with both: there may be two vortices, for instance, or the single one may be displaced to one side (*Famille neuropathique*, p. 259, 1898). P. Godin (*Compt. rend. Soc. de biol.*, 10 s., iv. 656, 1897) has noted hereditary transmission in relation to this malformation, and has described fistulæ in a father, his son, and two grandchildren; Lawson Tait (*loc. cit.*) had already referred to cases of sacral dimple in a mother and all her children. M. Salaghi (*Arch. di ortoped.*, xvi. 10, 1899) has pointed out that cysts developed in these foveolæ might be mistaken for spina bifida.

I have met with quite a number of sacral dimples in the series of over three hundred deformities which I have examined. They may, for instance, occur in association with spina bifida and with anencephaly. They are cutaneous invaginations; and they probably account not only for the sinuses and fistulæ which arise over the sacrum and coccyx, but also for the sequestration-dermoids of this region. Bland-Sutton (*Tumours*, p. 337, 1903) has compared these sinuses to the interdigital pouch of the lamb. The teratogenesis of sacral dimples has been already referred to; but it may be added that Cleland regards them as due to arrest of growth of the notochord (*Journ. Anat. and Physiol.*, xvii. 289, 1883; *Memoranda in Anatomy*, i. 185, 1889).

Miscellaneous Malformations of the Spine.

In addition to the anomalies already described, I may name some others; space forbids that I do more. There is the presence of a foramen at the root of the transverse process of the first dorsal vertebra (W. Gruber, *Arch. f. path. Anat.*, lxvii. 341, 1876; W. Turner, *Journ. Anat. and Physiol.*, xvii. 255, 1882–83; xviii. 223, 1883–84). There may be anomalies in the form and connections of the atlas and axis vertebræ (G. Sangalli, *R. Ist. Lomb. di sc. e lett.*, 2 s., iii. 515, 1870; W. W. Keen, *Amer. Journ. Med. Sc.*, n.s., lxvii. 412, 1874; G. Romiti, *Boll. d. Soc. tra i cult. d. sc. med. in Siena*, iv. 99, 1886; W. Turner, *Journ. Anat. and Physiol.*, xxiv. 358, 1889–90; H. Waterhouse, *Proc. Anat. Soc. Gr. Brit. and Ireland*, p. xxxiii., 1893). Persistence of the notochord in the lumbar region of the spine in an adult has been described by J. Musgrove (*Journ. Anat. and Physiol.*, xxv. 386, 1891). Half-vertebræ have been already referred to.

Malformations of the Spinal Cord.

Of the malformations of the spinal cord apart from spina bifida comparatively little is known. Doubtless ere many years go by there will be much work done in this direction. Meanwhile I may note that a *double canal* or *multiple canals* have been met with both in the human subject (J. Wagner, *Arch. f. Anat., Physiol., u. wissensch. Med.*, 735, 1861) and in the chick (G. Cutore, *Atti d. Accad. Gioenia* *di sc. nat. in Catania*, 4 s., xii. and xiii., 1898–1900); these have been found not to open into each other nor into the true central canal, although they may be lined by the same kind of epithelium. Duplication of the spinal cord has also been met with apart from spina bifida (F. Cecco, *Morgagni*, i. 307, 1857; P. Foà, *Arch. per le sc. med.*, xi. 423, 1887); and absence of some of the nerve roots would appear to be not uncommon (A. Adamkiewicz, *Arch. f. path. Anat.*, lxxxviii. 388, 1882).

I have recently seen sections of the spinal cord of a seven months' fœtus, which Drs. Matthew and Waterston were examining (*Rev. Neurol. and Psychiat.*, i. 233, 1903); in the cervical region it showed marked asymmetry from almost total *absence of the pyramidal fibres* on one side, and there was a fissure in the position where the fibres should have been found; in the medulla an explanation of the anomaly was found in the fact that at the level of the decussation of the pyramids the crossing of fibres took place from one side only. This, then, was an instance of heterotopia of the white columns of the cord.

Several cases of *heterotopia of the grey matter* in the spinal cord are on record. The grey matter may be found in separate masses or in parts of the cord which normally do not contain it (*e.g.* between the white columns). P. Kronthal (*Neurol. Centrlbl.*, vii. 97, 1888) described a case of this kind, and drew together out of literature a number of other instances. H. T. Tooth (*Trans. Path. Soc. Lond.*, xlii. 14, 1891) and C. M. Campbell and W. Aldren Turner (*ibid.*, p. 20) also described cases; in one of these there was general paralysis and in the other myelitis. It does not appear that the cord anomaly gives rise to symptoms by itself, but it would seem to predispose to diseases such as myelitis. There may also be marked asymmetry between the grey substance in the two halves of the cord, as was seen by P. Schiefferdecker (*Arch. f. mikr. Anat.*, xii. 87, 1875). Myelitis in fœtal life has been regarded as a cause of the heterotopia of the grey substance; by it the neuroblasts may be hindered from reaching their proper places (R. Fusari, 1896). Much more information, however, is needed before the vexed question of teratogenesis can be decided.

Distended cavities in the spinal cord may be met with, and these would appear to be due to localised dilatation of the central canal or *hydromyelia*. Hydromyelia occupies an ill-defined position in relation to two other morbid states, spina bifida and syringomyelia. Apparently it may sometimes exist alone without giving rise to any symptoms; at other times, as has been shown in Chapter XVII., it may either coexist with or be in causal connection with spina bifida; and at yet other times it may, according to some observers, be in intimate relation with syringomyelia. So strongly has the last-named relationship been believed in, that hydromyelia and syringomyelia have been used as synonymous terms (E. Leyden, *Arch. f. path. Anat.*, lxviii. 1, 1876). Other authorities think that syringomyelia is an acquired condition, due sometimes to injury to the cord, followed by hæmorrhages and the development of gliomata or myxogliomata and their subsequent degeneration (G. Hinsdale's article, *Internat. Med. Mag.*, v. 617, 681, 745, 1896–97). The two views need not be regarded as irreconcilable, for congenital hydromyelia and syringomyelia, although not identical, may yet be intimately related; and it may be supposed that gliomatous tissue will be prone to grow in cavities due to developmental defects. The reader who may wish to follow out these arguments must be referred to the special literature (now very considerable) of syringomyelia. Hydromyelia in relation to spina bifida and anencephaly has been specially studied by E. B. Block (*Contributions to the Science of Medicine, by the pupils of W. H. Welch*, p. 805, 1900).

The Antenatal Pathology of the Spine and its Contents is yet, as has been gathered, far from completely understood. Many problems still surround spina bifida, and, as has just been stated, the malformations of the spinal cord are full of difficulties of interpretation and causation. Observers and investigators will do well to remember that, on account of the late development of the nervous system, embryonic malformations and fœtal diseases are doubtless more intimately connected and more directly interdependent in the cord than elsewhere in the body.

CHAPTER XIX

Merosomatous Terata (*cont.*) : Malformations of the Cranium : Anencephaly or Acrania ; Definition ; Nomenclature ; Historical Notes ; Clinical Details ; Morbid Anatomy, Cranial Vault, Varieties of Defect, Face, Basis Cranii, Cerebral Structures, Eyes, Spinal Cord, Supra-renal Capsules, Sectional Appearances, Musculus Sternalis ; Associated Malformations ; Teratogenesis ; Literature.

In describing the malformations of the cranium and its contents I shall pursue the same plan as that adopted for anomalies of the spine, namely, I shall give fairly full details of one type of malformation, and little more than short notes of the other varieties. I have had little difficulty in deciding which type ought to be described at length, for the teratological state known as anencephaly or acrania has sovereign claims to be regarded as the master monstrosity of this part of the body. For one reason, it is, speaking relatively, a common monstrosity: few obstetricians who have attended more than two or three thousand labours have failed to meet with at least one instance of it; and in 325 cases of monstrosity and fœtal disease examined by myself there have been forty-six anencephalics, or 14 per cent. Again, it is a very striking monstrosity; and, yet again, it is an anomaly which suggests many interesting problems affecting the development and functions of the nervous system and its relation to the nourishment and growth of the body. Obviously, if any one monstrous state of the cranium is to be singled out for special description, anencephaly it must be.

Anencephaly (Acrania).

Anencephaly may be *defined* as that teratological state of the head in which the osseous vault of the cranium is more or less defective, in which the scalp is absent in whole or in part, and in which the brain is more or less gravely altered and may even be entirely wanting.

The *nomenclature* is somewhat complicated, for many more or less synonymous terms have been used to describe this monstrosity. In the early days anencephalic fœtuses were simply termed "cat-like" or "frog-like," or were more accurately described as "puellus" (or "puella") "sine cerebro natus" ("nata"). During the eighteenth century such deformities began to be called "acephalous" (*e.g.* by G. van Doeveren, *Specimen observ. acad. ad monstrorum historiam*, p. 46, Groningæ, 1765); but the name is erroneous, for they are not "headless" in the sense that the grossly defective twin fœtuses are "headless," and the latter alone ought to be termed "acephalic" or "acephalous."[1] Nevertheless the name thus unfortunately introduced has never been entirely abandoned; it is in use at the present day; and the expressions "spurious acephalus," "semiacephalus," and "hemicephalus" are, all of them, attempts (by Prochaska, Rossi, and Meckel respectively) to bring the terminology into correct relations with the morbid anatomy. Better names, however, were to be invented, and V. Malacarne (*Mem. Soc. ital.*, xii. pt. 2, p. 173, Modena, 1805) was fortunate enough to suggest the two expressions which have most successfully met the requirements of the case. These were the names "acrania" and "aencephalus"; and the latter in its more euphonious form, "anencephalus," is probably the most commonly employed at the present time. Neither of them is a perfect expression, for "acrania" concentrates attention upon the defective state of the bones of the head, and "anencephalus" refers only to the morbid condition of the cranial contents; but if the reader will keep them both in mind he will have a fair notion of the nature of the malformation for which they stand. At the same time neither of the names is to be taken in its literal signification: in "acrania" it is mainly the bones of the cranial vault that are absent, not those of the base; and in "anencephaly" the brain may not be entirely absent, but may be represented by a smaller or a larger portion in a less or more altered state. There are also the intermediate types or connecting links so troublesome to the taxonomist: in some cases, for instance, it is only the anterior part of the cranial vault that is absent, and in others the supra-occiput alone is at fault; and, again, there is no clear line of division between acrania and the different varieties of cerebral hernia (encephalocele, meningocele, etc.), although we may try to make the absence of the scalp over a greater or a smaller extent of surface the differentiating character.

The nomenclature, therefore, is not perfect. At the same time, I prefer the words "acrania" and "anencephaly" to such others as "cranioschisis," Förster's comprehensive term, and "crania bifida," which is little more than an attempt to establish a somewhat artificial bond of union between the present malformation and spina bifida. Some confusion exists; the fact is patent; my endeavour is not to increase it. I, therefore, employ "acrania" and "anencephaly" as synonymous expressions, intending to designate by them the group of malformations as a whole; other names to mark off sub-types will be introduced later.

It is an interesting fact in the *history* of this monstrosity that a specimen exists which is much older than the earliest reference to the anomaly to be found in literature. The mummy anencephalic fœtus found at Hermopolis in Egypt, to which I have already referred (p. 101), has obviously a much greater antiquity than the earliest record we possess, for it dates only from the sixteenth century. It is a curious fact that nothing which can be identified with anencephaly is to be found in the teratological lists of ancient Chaldea, although it seems very improbable that this monstrosity did not exist in Mesopotamia in these early times. The earliest recognisable account of an anencephalic fœtus would appear to be that given by Lycosthenes (*Prodigiorum . . . Chronicon*, p. 585, 1557). The author is enumerating the prodigies of the year 1544, and after referring to the birth of joined twins at Heidelberg, he proceeds as follows: "Quinto Calend. Septembris, Argentinæ nobilis Alsatiæ metropolis, infans fœminei sexus, horrendo, mostroso, atque in superiori parte, aperto plane capite, lato ore, bovinis oculis, naribus aquilinis natus est." The description and the illustration both point to this as a genuine instance of anencephaly, although we may be inclined, from what we know of present-day specimens, to doubt the presence of the "aquiline nose." In the same year, the chronicler goes on to tell us, "Henricus Anglie rex Gallos bello vexavit," a not unusual state of matters in these troublous times. Lycosthenes' case of anencephaly, "naribus aquilinis," has been followed by a long series of observations, so that Taruffi (*op. cit.*, vi. 95, 1891) had no difficulty in collecting together more than two hundred of them from medical literature, and one might with little trouble greatly increase the length of the list. It was not, however, till near the close of the eighteenth century that good descriptions of the anatomy of anencephaly began to be published, and the nineteenth century was well advanced before satisfactory theories of causation began to be advanced to explain the origin of the monstrosity. All the best known teratologists, such as Meckel, the Saint-Hilaires, Förster, Ahlfeld, Dareste, and Taruffi, have made important contributions to our knowledge of the subject; and the number of monographs and articles in journals has been very large and is ever increasing. In the present work I have already referred many times to anencephaly; indeed the consideration of the theories of teratogenesis in several instances resolved itself into the consideration of the theories of the production of anencephaly. Further, the monstrosity has already passed before the reader's eye in Figs. 25, 26, 27, 28, 32, and 33, and is represented also in Plates XXI. and XXII. It is partly by reason of its frequency that anencephaly has been described so often and so fully, for it has been said to occur once in 1460 labours, and, as has been stated already, I have had forty-six specimens of it put for examination into my hands during the past sixteen years; it is also a very arresting and wonder-provoking monstrosity.

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[1] The converse mistake of calling an acephalus "anencephalus" was made by J. B. Krombholz (*Anatomisches Beschreibung eines . . . Anencephalus*, Prag, 1830).

Clinical Details.

The pregnancy that ends in the birth of an anencephalic fœtus may be quite uneventful; but there is reason to believe that more often it is abnormal in one way or another. One cause which leads to the frequent association of some maternal distress with such a gestation is the very frequent presence of hydramnios as a complication. Indeed the symptoms that are noted in connection with it are generally those of hydramnios (J. Laulaigne, *Thèse*, Paris, 1883), over-distension of the uterus, interference with respiration and circulation, vomiting, pain in one side of the abdomen, etc. It is difficult to hear the fœtal heart, and when it can be heard it is irregular, slow, and weak, a character upon which G. Giglio (*Ann. di ostet.*, xix. 328, 1897) is inclined to rely for diagnostic purposes. On account of the excess of liquor amnii it is also difficult to palpate the fœtal parts and so to be sure of the cranial malformation. Hydramnios, however, is not constant, and I have met with at least two cases in which the opposite condition (oligohydramnion) was present; in such instances auscultation and palpation may be expected to be more helpful in diagnosis.

There is sometimes a history of abdominal traumatism during pregnancy, a fact which led the Saint-Hilaires to conclude that it had a causal connection with the malformation, and to which reference has already been made (p. 139). Further, maternal impressions are often alleged, an allegation which the resemblance of the anencephalic fœtus to a frog or a cat renders easy.

Family prevalence has been observed in connection with anencephaly. Two at least out of my forty-six cases were instances of this; in both of them the mother had previously given birth to an anencephalic fœtus, and in one the sex of the monstrosity was different (*Trans. Edinb. Obst. Soc.*, xxiv. 16, 1899). G. Lammert (*Arch. f. path. Anat.*, xxii. 230, 1861) has also noted this, and Carli (*Bull. d. sc. med. di Bologna*, 4 s., xix. 30, 1863) has reported the birth of three successive anencephalic fœtuses. J. Martin (*Med. Exam.*, Philadelphia, n.s., v. 23, 1840) put on record the extraordinary occurrence of six anencephalic births in the reproductive history of one woman; she had two normal infants and one other monstrosity. The monstrous infants do not always follow each other in successive pregnancies, for Bruneel's patient (*Ann. soc. méd.-chir. de Bruges*, 2 s., ii. 73, 1854) had fourteen labours, of which the fourth, twelfth, and fourteenth resulted in the birth of an anencephalic fœtus. Occasionally an anencephalic fœtus is born with a healthy co-twin, as in A. Paterson's case (*Trans. Edinb. Obst. Soc.*, iv. 376, 1878) and in Blandin's (*Journ. hebd. de méd.*, i. 107, 1828), or with a hydatid mole (P. Pagello, *Giorn. veneto di sc. med.*, 2 s., i. 636, 1853), or with a fœtus papyraceus (Curatulo, *Policlinico*, i. 379, 1894; *Ann. di ostet.*, xvii. 287, 1895). One of triplets has also been found to be anencephalic (namely, case reported by Plancus and cited by Taruffi, *Storia*, vi. 148). Further, both twins may be anencephalic, as in Otto's remarkable case (*Monstrorum Sexcentorum Descriptio*, obs. xlix. 32, 1841), in which they were both males and were born at the seventh month to a young primipara. In fused or conjoined twins, also, this monstrosity may be met with: instances are found in F. Nöll's specimen, a hemicephalic male fœtus with epignathus (*Diss. inaug.*, Marburg, 1882), in F. G. Parsons' case, a male anencephalous fœtus with three arms and three lower limbs (*Journ. Anat. and Physiol.*, xxx. 238, 1896), and in S. T. Sömmerring's four examples of dicephalic monstrosities (*Abbildungen und Beschreibungen einiger Misgeburten*, Plates iii., v., vi., vii., Mainz, 1791). It may be noted as a fact of some possible importance that in the reproductive history of a woman who has had an anencephalic monster there may be the record of the earlier or a later birth with hydrocephalus or spina bifida; I have met with two or three instances of this. An anencephalic fœtus has been carried in a bilocular uterus (P. L. Gardini, *Ann. di ostct. e ginec.*, xxi. 705, 1899); it has also been found in a tubal gestation sac (*Centrlbl. f. Gynäk.*, xxv. 385, 1901). Finally, the manner in which anencephalic fœtuses occur in groups in general obstetric practice may be referred to simply as a matter of curiosity. P. Del-Vesco (*Gazz. med. ital. prov. venete*, Padova, ii. 149, 1859) had the following extraordinary experience: for nine years in practice he never saw a single monstrosity, then within twelve months he assisted at the birth of five anencephalic fœtuses; there followed a period of three years without teratological manifestations, then within one month he met with three anencephalics; eight years then elapsed during which he saw no further cases. I have had no experience like this, but I have received two very similar specimens of pseudencephaly (Figs. 25 and 26) from different parts of the country within twenty-four hours, and I have on several occasions had two anencephalics handed to me within a few days; but these are commonplace occurrences compared with Del-Vesco's.

It would seem that the anencephalic fœtus is usually of the female sex. At any rate there are thirty females and only ten males in my collection of forty-six anencephalics; the remaining six cases may have been either males or females, the fact was not noted or else only the upper part of the body came into my hands. Meckel (*Handbuch der path. Anat.*, i. 234, 1812) found a somewhat less marked excess of females over males (44 : 36). Förster (*Die Missbildungen des Menschen*, p. 81, 1865) doubts its greater frequency in either sex; but it seems to be a well-established fact.

The birth of an anencephalic fœtus is not necessarily rendered difficult by the malformation; but the malformed state of the head makes a malpresentation more probable and so may introduce delay, and the frequent coexistence of hydramnios may cause uterine inertia and predispose to hæmorrhage. Further, when the malformed head presents it does not fit accurately into the pelvic brim, and on this account the cord or the hands may prolapse; again, it acts as an unsatisfactory dilator, and so delay is caused; and again, even when the head is born there may be retardation in the birth of shoulders, requiring the division of one or both clavicles (cleidotomy). It would seem, also, that the labour is apt to be complicated in other ways, *e.g.* by placenta prævia, as in a case recently reported by myself (*Journ. Obstet. Gynæc. Brit. Empire*, v. 148, 1904).

Several interesting questions group themselves round the phenomena of life manifested by the anencephalic fœtus. That they live in utero, of course, is evident; further, they move freely inside the uterus even when the spinal cord as well as the brain seems to be entirely absent, as in one of the cases shown by myself in 1898 (*Trans. Edinb. Obst. Soc.*, xxiii. 83, 1898). More than this, their life in utero may be unduly prolonged, for although most anencephalics have been born prematurely some have come postmature into the world. I think it is possible that the postmature anencephalics may owe their longer sojourn in the uterus to absence of excess of liquor amnii; at any rate in the three cases which I have met with in which anencephaly and postmaturity were associated there was no evidence of hydramnios (*Journ. Obstet. Gynæc. Brit. Empire*, ii. 530, 1902).

When an anencephalic fœtus is born alive it usually quickly succumbs; but some remarkable instances have been reported of continued postnatal life. This is more likely to occur when the labour is at the full term, when the whole brain is not absent, and when part at least of the cranial vault is intact; but even in cases of complete absence of vault and cranial contents signs of vitality may continue for some minutes or even some hours. Instances of the postnatal life of anencephalics have been recorded by Burrows for six days (*Med.-Chir. Trans.*, 3rd ed., Lond., ii. 52, 1817), by Polaillon for twenty-four hours (*Bull. Soc. de chir. de Paris*, 3 s., iii. 435, 1874), by S. S. Purple for two and a half days (*New York Journ. Med.*, n.s., v. 40, 1850), by W. Lawrence for four days (*Med.-Chir. Trans.*, Lond., v. 165, 1814), by C. Lucia for thirty-four hours (*Siglo méd.*, Madrid, iii. 187, 1856), by A. A. Spessa for eleven hours (*Ann. univ. di med.*, lxiv. 189, 1832; *Gaz. méd. de Paris*, 2 s., i. 46, 1833), and by Stapfer for at least an hour and a half (*Ann. de gynéc.*, xxiii. 127, 1885). W. Ross's case (*Trans. Obst. Soc. Lond.*, ix. 31, 1868) would seem to have lived for more than sixteen days.

The vital phenomena which have been shown by anencephalic fœtuses after birth have excited considerable interest; and they proved puzzling in the extreme to the physiologists of the past, who did not realise the capabilities of the spinal cord. Purple (*loc. cit.*) watched his case carefully, and noted that it breathed as soon as it was born although inspiration was spasmodic in character, that the skin of the face and chest and the eyes became congested for a time, that deglutition was at first somewhat difficult, that it sucked with considerable force, that its pulse was irregular and slow (68 to 76 per minute), that it passed urine and fæces freely, and that they were natural, that it made frequent and partly successful efforts to cry, and that it made convulsive movements when its skin was pinched or the deformed cerebral mass touched. The temperature was normal.

In a well-marked case of anencephaly seen by Saviard (*Observations chirurgicales*, p. 257, Paris, 1702) the infant lived for four entire days; it opened and closed its eyes, it cried, it took the breast, and it swallowed the milk. Another infant (*op. cit.*, p. 249) lived for six hours, often opened its eyes, especially the left, and swallowed a little sugar and wine. John Heysham's female anencephalic child (Duncan's *Medical Commentaries*, Dec. 2, iii. 429, 1789) lived for five days and twenty-one hours; she swallowed nourishment well, moved her limbs "with apparent agility," cried, and had slight convulsions for some time before her death. The excrescence upon the basis cranii, after the most accurate post-mortem examination, showed not the smallest trace of a brain. "This," says Heysham, "may justly be considered as a very curious, and perhaps an important circumstance in physiology." So, in effect, say also N. Vaschide and C. Vurpas, who in recent years have turned to the study of the biological phenomena of the anencephalic fœtus, bringing with them all that modern physiology can give to help in the solution of the problem (*Compt. rend. Acad. d. sc.*, cxxxii. 641, 1901; *Nouv. iconogr. de la Salpêt.*, xiv. 388, 1901). A male infant, with no trace of cerebral hemispheres or cerebellum, with an incomplete medulla and pons, with some rudiments of the corpora quadrigemina, and with an apparently normal spinal cord, was born at the tenth month, was resuscitated, and lived for thirty-nine hours. During his short life he had a low rectal temperature (95° F.); his respirations were nine per minute, and of a marked Cheyne-Stokes type; the pulse was 138, with some intermissions during inspiration; his skin was cyanosed; his patellar reflex was difficult to elicit owing to the contracted state of the legs, but the reflexes of the forearms were exaggerated; idiomuscular reflexes were also present; the eyes were prominent; and there was very pronounced external strabismus and dilatation of the pupils. There was, however, immobility of the pupils and absence of reaction even to bright light. He sucked and swallowed, and drew the body away when the skin was pinched or pricked or heated. He made a few cries. There seemed to be no sense of taste (*e.g.* for quinine), and camphor did not seem to affect the nasal mucous membrane, but the vapour of ammonia made him draw back his head. Loud sounds and bright lights had no apparent effect. Twenty hours after birth he began to have convulsions; these began in the left upper limb and were soon general, being followed as a rule by micturition. The case presented a number of very puzzling problems, such as the origin of the spontaneous and associated movements, the normal character of the muscles (absence of atrophy, etc.) in the presence of such a defective cerebro-spinal nervous system, the cause of the signs of intense inflammatory change in the nerve tissues, membranes, and vessels. Vaschide and Vurpas evidently hesitated to draw conclusions from these data which would be contradictory to established beliefs in the action of the nervous system, and dreaded advancing "adventurous hypotheses." At the same time it is clear that physiologists must find explanations for these facts; for it is no longer possible to say, as Duncan did (in 1789) about Heysham's observation, that "a case so singular can hardly be supposed to warrant any general conclusion whatever."

Morbid Anatomy.

In anencephaly the cranium is the part most affected, so I shall consider that region first. The cranial vault bones and the scalp covering them may be absent in part or in whole: it is upon this character that Taruffi (*op. cit.*, vi. 117, 1891) founds his primary division of all specimens of the monstrosity into *mero-acrania* (partial absence of vault, with protrusion of cranial contents) and *holo-*

acrania (complete absence of vault, with loss of cerebral tissues). The former group corresponds with the exencephalic and partly with the pseudencephalic families of Isidore Saint-Hilaire, and the latter with that writer's anencephalics proper and partly with his pseudencephalics (*Histoire des anomalies*, ii. 293–374, 1836). Mero-acrania also corresponds with A. Spring's group of "ectopia of the cerebrum" (*Mem. Acad. roy. de méd. de Belgique*, iii. 179, 1854).

Cranial Vault.

According to the position and extent of the cranial defect Taruffi obtains secondary divisions of mero-acrania. When it involves the frontal plates alone he calls it (1) *anterior mero-acrania*: in this type, which is rather rare, the margins of the parietals are usually slightly affected, the orbital plates of the frontals are commonly present, the rest of the vault is flattened, and the supra-occiput below the protuberance is perpendicular. It corresponds with *proencephalus* of Saint-Hilaire. In (2) *median mero-acrania* (*podencephalus*, Saint-Hilaire) the upper part (vertex) of the cranium is defective, and the greater part of the contents lies outside; the bones chiefly affected are the parietals, but the contiguous margins of the frontal plates and of the supra-occiput may likewise be defective, and the temporals are approximated anteriorly. Thus a diamond-shaped opening in the vault is produced, the shortest diameter of which is the antero-posterior. This type is, like the former, comparatively rare, and Taruffi enumerates only thirteen specimens. Among these is the case reported by W. Ross (*Trans. Obst. Soc. Lond.*, ix. 31, 1868), a negro infant, in whom there was considerable arrest of development of the parietal and temporal bones; the frontal bones and the lower jaw were well formed, but the superior maxilla was deformed, as were also the fingers and toes. The monster lived for more than sixteen days. A coloured plate accompanies the record. Spina bifida does not appear to be associated with this form of acrania.

A third variety of mero-acrania is called *antero-median* by Taruffi (*op. cit.*, vi. 121, 1891). In it both the parietals and the frontals are largely absent; it is thus similar to the former type save in the larger extent of the osseous defect. The name nosencephalus ("morbid brain") was given to it by Saint-Hilaire, but it is somewhat inexact. About ten cases have been reported, including one by F. P. L. Cerutti (*Rarioris monstri . . . descriptio*, Lipsiæ, 1827), in which, in addition to the cranial deformity, there were facial fissures, ectopia cordis, and other malformations, the whole picture drawing from the author (not without reason) the exclamation, "En mirabile visu monstrum!" In another instance, that reported by P. Pézérat (*Journ. compl. du dict. d. sc. méd.*, xxix. 252, 1827), the right arm was absent, the parietals were entirely absent, and the frontal plates were represented only by two osseous fragments. Under the somewhat cumbersome and ambiguous name, "*antero-tubercular mero-acrania*," Taruffi has placed together seventeen specimens in a fourth group; in them the whole cranial vault was absent save that part of the occiput lying below the level of the occipital protuberance. They correspond roughly to Saint-Hilaire's division of the *hyperencephalics*, and they are more numerous than any of the previously named types. A good example was well described by L. Heydenreich (*Arch f. path. Anat.*, c. 241, 1885): the exposed brain consisted of three lobes covered with the membranes, there was also a median fissure of the face, and amniotic bands were attached to the stunted fingers; the author is inclined to ascribe all the deformities to the amniotic adhesions. Taruffi has constructed a fifth and final group of mero-acranial monsters with the name *postero-spinal*: its leading character is absence of the supra-occiput, extension of the foramen magnum, an open condition of the cervical (and sometimes of the dorsal) spine, and flattening of that part of the cranium roofed in by the frontals and parietals; and it includes Saint-Hilaire's genera of *iniencephalus*, *exencephalus*, and *notencephalus*. It has seemed to me more convenient and correct to consider this as a teratological state by itself and quite separate from anencephaly; I have, therefore, described it in Chapter XVI., to which I now refer the reader.

Leaving out of account the cases of iniencephaly (postero-spinal mero-acrania), it may be said that mero-acrania is rarely associated with spina bifida, although there may be anomalies of other kinds affecting the vertebræ. In *holo-acrania*, on the other hand, spina bifida is practically constant. In complete acrania ("holo-acrania," as Taruffi prefers to call it) the whole vault of the cranium is absent: the parietals, the squamous parts of the temporals, the frontal plates, and the supra-occiput including the foramen magnum are all wanting, although sometimes remnants of these bones are turned backwards and downwards at the sides of the basis cranii, where they project like wings or horns. When the basis cranii is uncovered by either nervous or vascular tissue and simply shows a more or less thickened membrane (dura mater) Saint-Hilaire called the condition *anencephalus*, although he also used the same name for the larger group; when the base is covered by a spongy, vascular mass he named it *pseudencephalus*; when the vascular mass is present along with a very minor degree of cervical spina bifida it was *thlipsencephalus*; and when there is spina bifida and absence of the spinal cord only in the cervical region it was *derencephalus*. Obviously, these varieties are refinements of classification and unnecessary for ordinary purposes. A few words, however, may be said regarding the kind and degree of spina bifida or rhachischisis which accompanies holo-acrania. There may, for instance, be an open spinal canal all the way down the back, constituting a gutter with everted edges and shallow everywhere save sometimes in the cervical region where a lordotic curve of the vertebral bodies may exist. The gutter may be covered simply with a layer of dura mater, or it may contain a tube of spinal membranes, or it may show some nervous filaments or a duplicated spinal cord. Again, the spina bifida may affect only the dorsal and cervical regions, and in these regions the cord is commonly absent, although it may be present lower down. Yet again, the open state of the spine may exist only in the cervical region; indeed, only the first two cervical vertebræ (even the atlas alone) may be imperfect. Sometimes the division of the spine may affect the vertebral bodies (anterior spina bifida) as well as the arches, and this gives rise to what has been called "anencephalus perforatus." I have seen one specimen of this, and in it there was also exomphalos and absence of the symphysis pubis, with the result that a fœtus was produced whose two lateral halves were united almost solely by the basis cranii (Specimen No. 28).

Face and Basis Cranii.

I now pass to the description of the other parts of the head in anencephaly (the basis cranii and the face). The absence of the cranial vault gives to the face an appearance of breadth, but, as a rule, the whole head is rather small, all the diameters of the base being diminished. In a female anencephalic fœtus (Fig. 57) measuring 38 cms. in length I found that the "occipito-frontal" diameter was 5·5 cms., the "occipito-mental" 6·8 cms., and the transverse both in front of and behind the ears was 6 cms.; the transverse measurement of the face between the malar bones was 5·5 cms., and the vertical or "fronto-mental" was 6 cms. In this instance the transverse diameter of the shoulders was only 4 cms., but it is common for it greatly to exceed the corresponding head diameter; in fact, the broad shoulders usually form an obstacle in the delivery of the anencephalus. The face is prominent, partly on account of the thick layer of fat which covers the cheeks, and partly by reason of the projection of the lower jaw (its hyper-prognathism). For the relation of the lower to the upper jaw it will be well to contrast Plate XIX. with Plates XXI. and XXII.

The eyes are large and seem to bulge out of the orbits (which are shallow); and in the typical anencephalic they look almost directly upwards, hence the somewhat fanciful name "uranoscopic" (star-gazing) given sometimes to this type of monstrosity. The eyelids are often thick and œdematous in appearance. The nose is almost always flattened, and the mouth is generally open, with the tongue protruding (Plate XXI.). The ears have a twisted and deformed appearance and rest on the shoulders; the auditory meatus passes downwards and forwards. There is no forehead, the eyes and root of the nose forming the upper limit of the face.

The head is deeply set on the shoulders and the skin of the face commonly passes directly on to the chest, there being no indication of a neck groove. This is not constant, for now and again we meet with a specimen in which there is a slight sulcus and sometimes with one in which there is a true neck, but they are rare. The anatomical cause of the neckless appearance will be referred to immediately.

The basis cranii as studied by sectional and dissectional methods shows various anomalies. It may look directly upwards (as in Fig. 57, and in one of Bauer's cases, *Diss. inaug.*, Marburg, 1863), or partly upwards and partly backwards (as in Plate XXII.), or almost directly backwards (as in Plate XXI. and Fig. 58). The last-named arrangement is the most typical, and probably represents the least degree of commencing retroflexion of the spine (which is so often combined with anencephaly, *vide* Fig. 28). There is an advanced degree of ossification observable in the bones of the base: the presphenoid and basi-sphenoid are commonly fused together into one bone, and this may likewise be merged with the osseous basi-occiput (Fig. 57), but not constantly (Fig. 58, and Plate XXI.). The petrous parts of the temporals are short and thick, and may be fused with the sphenoid to form a large keystone in the centre of the base of the cranium. The squamous temporals and also the tympanic rings are commonly entirely absent. The stapes may not reach the fenestra ovalis (T. Biancini, *Di una anencefalia,* Pisa, 1829), and may be deformed (A. Wallmann, *Arch. f. path. Anat.*, xi. 503, 1857[1]); and various other anomalies of the internal ear (of the tympanic cavity, of the cochlea, vestibule, and semi-circular canals) have been described (R. Voltolini, *Monatschr. f. Ohrenhlk.,* iv. 111, 1870). In one of my specimens (*Journ. Anat. and Physiol.,* xxvi. 516, 1892) there was no condyle on the petrous part of the temporal for articulation with the lower jaw, and in its place was a small spine which projected between the coronoid process of the jaw and a projection representing the neck of that bone below the condyle, for the condyle itself was absent. The malar bones, in this case, were large, and each articulated with the external angular process of the frontal and with the great wing of the sphenoid, but not directly with the zygoma of the temporal. The external angular process of the frontal articulated with the zygomatic process of the temporal. Doubtless these anomalies are not present in all anencephalics.

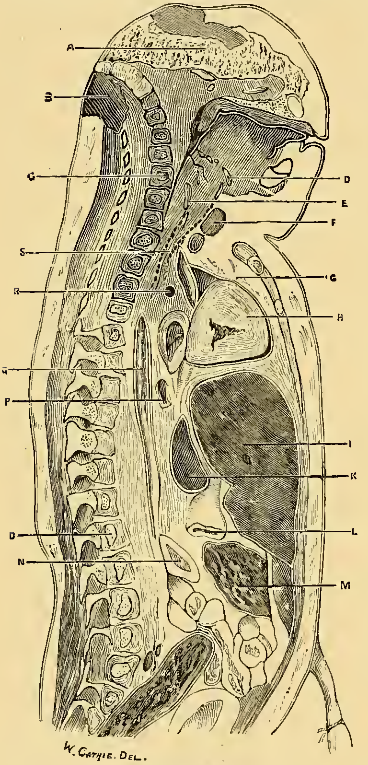

Fig. 57. — Vertical Mesial Section of Head and Trunk of Anencephalic Fœtus (left face shown and reduced one-half). A, bones fused together to form basis cranii; B, spina bifida; C, 7th cervical vertebra; D, hyoid bone; E, cricoid; F, thyroid gland; G, thymus; H, heart; I, liver; K, lobus Spigelii; L, pylorus; M, transverse colon; N, third part of duodenum; O, second lumbar vertebra; P, œsophagus; Q, aorta; R, right pulmonary artery; S, trachea.

To return to the description of the sphenoid, it may be found that the great wings are rather stunted, and that the small wings are

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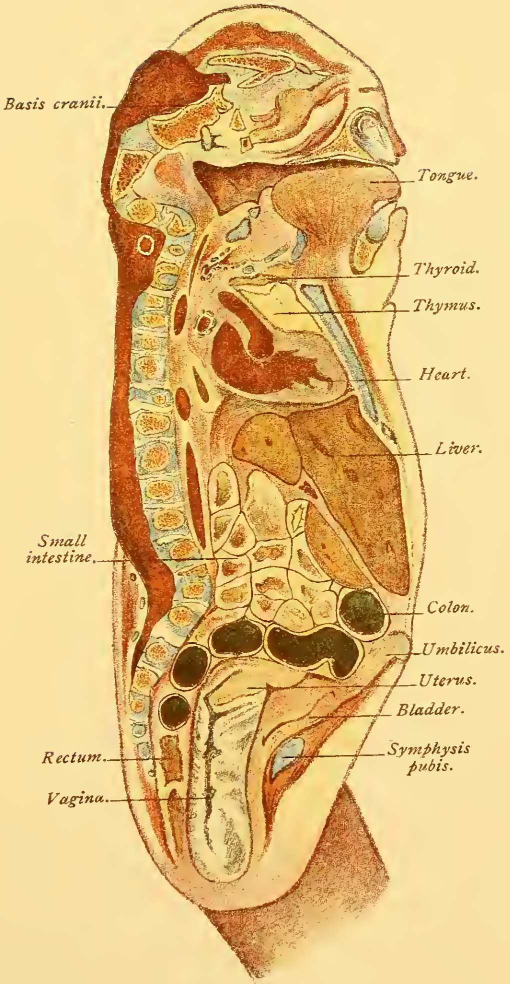
[1] The *Index Catalogue* gives the year as 1856, one of the very few inaccuracies I have detected in this fine work.

PLATE XXI


Basis cranii.
Tongue.
Thyroid.
Thymus.
Heart.
Liver.
Small intestine.
Colon.
Umbilicus.
Uterus.
Bladder.
Symphysis pubis.
Rectum.
Vagina.

either absent or fused with surrounding parts (perhaps with the orbital plate of the frontal, as in one of my specimens in which the frontal bone was represented by the nasal spine and posterior part of the orbital plates). The pterygoid processes, if present, may be deformed. The fusion of the pre-sphenoid and basi-sphenoid has been referred to already. The single bone thus produced may lie in the same plane with the basi-occiput (Fig. 57); but more often it forms a sharp angle with it (Plates XXI., XXII.; Fig. 58), so that while the upper surface of the sphenoid may look upwards, that of the basi-occiput is directed backwards. The depression of the sella turcica is thus usually entirely effaced. Some very ingenious theories regarding the sphenoidal angle and its mode of production in anencephaly have been advanced by F. G. J. Bauer (*Diss. inaug.*, Marburg, 1863), by C. T. Ackermann (*Die Schädeldifformität bei der Encephalocele congenita*, Halle a. S., 1882), by W. Quicken (*Diss. inaug.*, Halle a. S., 1885), and by C. Taruffi (*Storia della teratologia*, vi. 111, 1891). It is unnecessary to consider these theories in detail; but it would appear that the sharpness of the angle between the sphenoid and the basi-occiput depends greatly upon whether there is holo-acrania or mero-acrania. In the latter case, and especially when the mero-acrania is anterior or median, the angle may be much less marked. Sometimes the basi-occiput, instead of being bent downwards from the sphenoid, may be flexed upwards upon it. The change in the direction of the basis cranii is intimately connected with the presence of lordosis of the cervical part of the spine. The degree of the lordosis varies greatly, but there is nearly always lordosis and very rarely cyphosis (Fig. 58). The cervical lordosis accounts, also, in large measure, for the neckless state of the anencephalic fœtus; but cyphosis has the same effect. The only specimen of anencephaly which I have met with which possessed a distinct neck had a spinal canal closed right up to the occiput, so that the presence of spina bifida would appear to have much to do with this neckless state. The cervical vertebræ are often reduced in number, fused together, or otherwise abnormal, circumstances which also tend to shorten the neck.

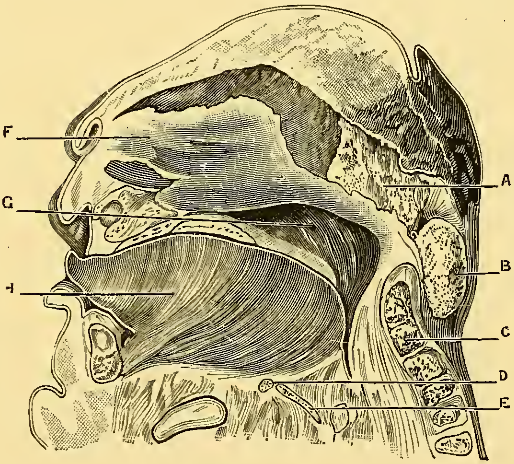


Fig. 58.—Vertical Mesial Section of Head of Anencephalic Fœtus (right face shown, natural size). A, sphenoid; B, basi-occiput; C, body of axis vertebra; D, hyoid bone; E, thyroid cartilage; F, septum of nose; G, Eustachian tube; H, tongue.

Cerebral Structures.

Turning now to the structures found lying on the basis cranii or contained within the rudimentary cranial cavity, I may state that great differences exist. As a rule, the more complete is this absence of the cranial vault the less likely is it that any nervous tissue will be found on the base; in such cases of holo-acrania not even a membranous sac may be found, and all that is present is a layer of tissue (dura mater?) with some vascular portions (pia mater?) adhering to it and covering the bones. Rarely in holo-acrania and commonly in mero-acrania a spongy mass of tissue is seen occupying the position of the brain (*pseudenecephaly*): this consists of a sac made up of the more or less altered cerebral membranes and containing more or less altered cerebral substance. The sac, according to Bauer (*op. cit.*), has an external, smooth surface consisting of connective tissue adhering to the dura mater, which contains no sinuses; occasionally the smooth surface is lost and in its place are membranous fragments or filaments which had attached it to the amnion. On the inner surface of the sac-wall it is difficult to trace a distinct arachnoid membrane. The contents may consist of greatly softened cerebral substance, infiltrated with blood, but in which, occasionally, definite parts of the brain can be made out. In other cases they are made up entirely of a red spongy "fungous" substance, consisting of a network of connective tissue in which are numerous vessels distended with blood. These vessels may show aneurismal swellings, and doubtless they are derived from the pia mater and really represent the cerebral arteries and veins. In yet other instances the interstices of the network are filled with serum or the tissue itself is converted into one or more cysts with clear contents. In F. G. Gade's anencephalic fœtus, the third born to the same mother, there were some traces of the pituitary body (*Norsk. Mag. f. Lægevidensk.*, 4 R., ix. 715, 1894); but these are rarely seen. In Vaschide's specimen (*loc. cit.*) the corpora quadrigemina were recognisable, as was also the medulla oblongata, but in the latter organ the restiform bodies, the inferior olive, and the arciform fibres were wanting. It is quite the exception for distinct traces of any parts of the nervous system above the level of the medulla to be met with in anencephaly. It is, on the other hand, not uncommon to recognise some of the cranial nerves lying on the basis cranii (H. Mattersdorf, *Diss. inaug.*, Berlin, 1836). They either lie with free blunt or tapering ends on the bones or are inserted into the membranous sac; and they may or may not contain nerve fibres. The cerebral vessels usually show marked anomalies. The circle of Willis is not complete; the carotid arteries are small or follow an unusual course; and the vertebral arteries may be obliterated. It has to be noted, however, that exceptions occur, for the carotids and vertebrals may have their usual arrangement and be of normal calibre (*Bauer*).

The Eyes in Anencephaly.

Several observations have been made upon the eyes of anencephalic fœtuses, for the fact could not pass unobserved that these organs often had a perfectly normal appearance, although, of course, they had no connection with a brain. Eduardus de Wahl (*Diss. inaug.*, Dorpati Livonorum, 1859) examined the microscopic characters of the retina in a case of anencephaly and amyelia; W. Manz (*Arch. f. path. Anat.*, li. 313, 1870), C. Ritter (*Arch. f. Augenh.*, xi. 215, 1881–82), Joseph Hegler (*Diss. inaug.*, Würzburg, 1893), F. G. Gade (*loc. cit.*), and Vaschide and Vurpas (*Compt. rend. Acad. d. sc.*, cxxxiii. 304, 1901) made similar investigations. Gade found, as might be expected from the close relations existing between the brain and the eye, that the lens, the cornea, the ciliary body with the iris, and the ganglionic layer of the retina were absent, and that, in one eye, there was coloboma of the retina and choroid. The specimen of Vaschide and Vurpas, however, gave very different results: to the naked eye the organ was normal, and under the microscope the retina showed wonderfully little change; even the layer of rods and cones existed (although not so distinct as usual). It is evident that another puzzling problem in Embryology and Physiology arises in connection with the eyes of the anencephalic fœtus.

Spinal Cord in Anencephaly.

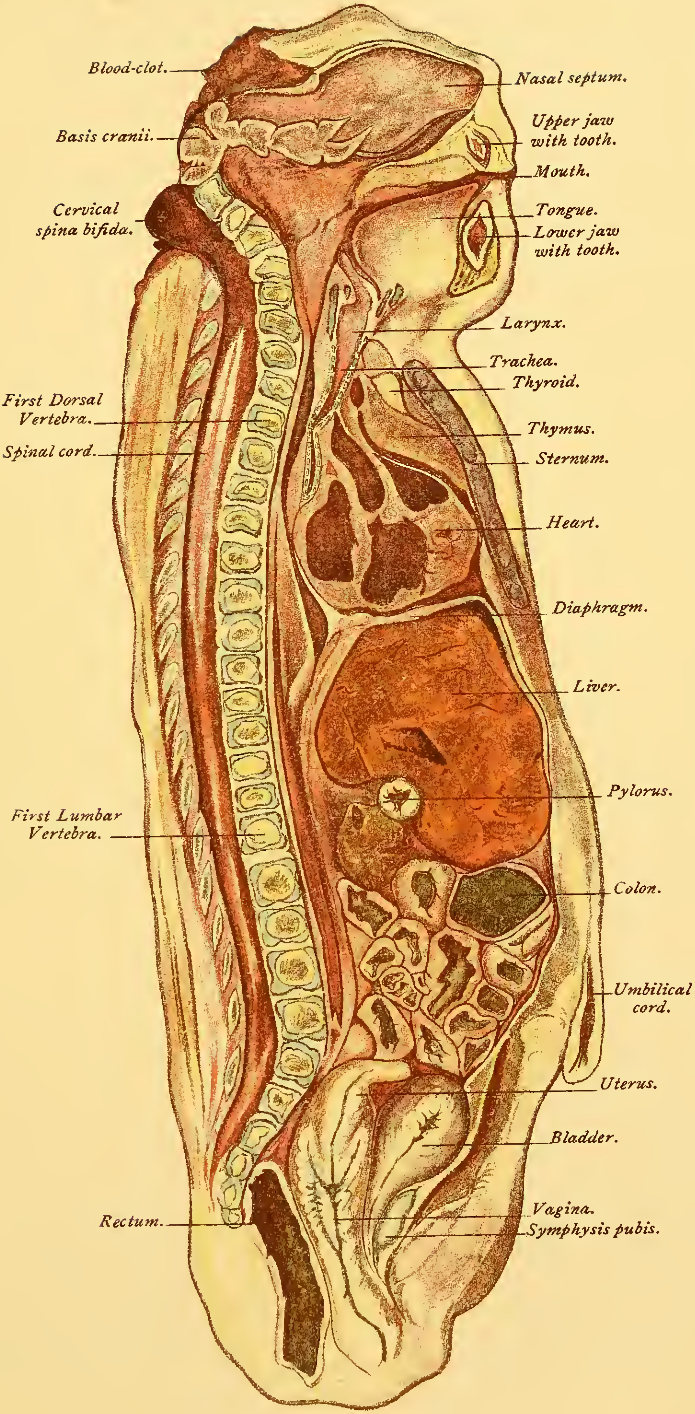
The condition of the spinal cord, like that of the brain, varies greatly in different specimens of anencephaly; indeed, much that has been said regarding the cord in spina bifida might be repeated here. There may be practically no trace of a cord, or there may be all the gradations between entire absence (amyelia) and a nearly perfect structure. Within recent years three careful histological examinations have been made: those of Bulloch (*Journ. Anat. and Physiol.*, xxix. 276, 1895), of Vaschide and Vurpas (*Nouv. iconogr. de la Salpêt.*, xiv. 388, 1901), and of D. Waterston and E. Matthew (*Rev. Neurol. and Psychiat.*, i. 465, 1903). In Bulloch's case (in which the upper part of the cord was wanting) the white matter in the cord was small in proportion to the grey, the anterior horn contained normal multipolar ganglion cells, Clarke's column contained very few cells, and the lateral horn of the dorsal region was quite rudimentary; with regard to the white matter, the pyramidal, direct cerebellar tracts, and the tract of Lissauer were absent. In Vaschide's specimen there was a degenerated condition of the nerve cells in the anterior horn; the white matter was small in amount (the lateral cords being especially reduced); there was an increased number of neuroglia cells and signs of intense inflammatory action (dilated blood spaces); just behind the anterior fissure fibres could be seen passing from one anterior horn to the other; and the nerve roots were practically normal; in this instance there were some traces of the mid-brain. In the specimen of Waterston and Matthew there was no nervous tissue above the medulla oblongata; the cord showed normal cervical and lumbar enlargements; in the sacral and lumbar parts the lateral columns of white matter were small, but the motor cells of the anterior horns were large and well developed, and the central canal was fairly well formed; in the dorsal region there were numerous blood vessels of large size and masses of red blood cells resembling hæmorrhages in both the white and grey matter, the lateral columns were much diminished and their surface fissured; in the cervical region there were two (and at one part, three) distinct central canals, the direct and crossed pyramidal tracts were absent, and there was no fissuring of the surface over the lateral columns, perhaps on account of the presence of many commissural fibres. It is evident, therefore, that the histology of the cord in anencephaly differs considerably; it also contains problems for the neurologist of a somewhat complex kind, as Vaschide and Vurpas (*Compt. rend. Acad. d. sc.*, cxxxiii. 116, 1901) clearly point out.

The *supra-renal capsules* in anencephaly are often found to be wanting (seven times in seventeen specimens, according to R. Lomer, *Arch. f. path. Anat.*, xcviii. 366, 1884), and in other instances they are diminished in size (Bender et Léri, *Compt. rend. Soc. de biol.*, lv. 1137, 1903). I have noted these facts in some of my specimens, and in one case (*Journ. Anat. and Physiol.*, xxvi. 516, 1892) the left adrenal was absent while the right was present. These organs, however, are not constantly affected in anencephaly; they may be normal. In this connection, observations have also been made upon the sympathetic system in anencephaly. Thus, in a case in which the supra-renal capsules were incompletely developed, C. Weigert (*Arch. f. path. Anat.*, c. 176, 1885) found that the superior cervical ganglion of the sympathetic was absent; but the association of the two defects is not constant, as Weigert himself showed (*Arch. f. path. Anat.*, ciii. 204, 1886). Karl Biesing (*Diss. inaug.*, Bonn, 1886) also investigated the supra-renal capsules and sympathetic system in anencephaly; he examined nineteen fœtuses (ten females and six males, three unknown), and found a greater or less degree of defective development of the adrenals in them all, but the degree of defect was not in proportion to that of the skull; the sympathetic cord was unaltered in all the cases. It may be concluded, therefore, that while there exists some relation between absence of the brain and defective development of the supra-renal capsules, the state of the sympathetic system is not necessarily influenced by that of the cerebro-spinal. Herein is one other problem for embryologists and physiologists to give their attention to.

Sectional Appearances in Anencephaly.

Eighteen out of my forty-six specimens of anencephaly were studied by means of frozen sections, and some of the sections have been reproduced for this work (Plates XXI., XXII.; Figs. 28, 57, 58) and in journal articles (*Physician and Surgeon*, i. 891, 1900; *Journ. Obstet. Gynæc. Brit. Empire*, ii. 521, 1902). It is unnecessary that I discuss in detail the various parts of the regional anatomy of anencephaly; but I may refer to one or two matters of special interest. In sixteen of the cases in which the sectional method was followed it was possible to note the curvature of the spine in its

PLATE XXII.


Blood-clot.
Basis cranii.
Cervical spina bifida.
First Dorsal Vertebra.
Spinal cord.
First Lumbar Vertebra.
Rectum.
Nasal septum.
Upper jaw with tooth.
Mouth.
Tongue.
Lower jaw with tooth.
Larynx.
Trachea.
Thyroid.
Thymus.
Sternum.
Heart.
Diaphragm.
Liver.
Pylorus.
Colon.
Umbilical cord.
Uterus.
Bladder.
Vagina.
Symphysis pubis.

whole extent. In fifteen of these there was cervical lordosis: it was marked in six cases, extraordinarily marked in one (Fig. 28), and slight in one, while in the remaining seven it was quite recognisable; in the sixteenth case the whole spine, including the cervical region, was practically straight. In no instance was there cervical cyphosis, although this has been noted by other observers (*e.g.* Taruffi, *Storia della teratologia*, vi. 104, 1891). In eight of the sixteen cases there was dorsal cyphosis, and in five of these the cyphosis was slight; in seven the dorsal region was straight or nearly so; and in one only was there lordosis in the upper and cyphosis in the lower dorsal region. In eight instances there was lumbar lordosis; in three there was cyphosis, and in five the lumbar region was straight or nearly so.

Another fact brought out by the sectional anatomy was that the structures in the neck all lay at a lower level in relation to the cervical vertebræ than is usual in the fœtus (although not in adult). The organs in the upper part of the thorax also lay at a lower level *quâ* the spine; in the abdomen there were often alterations in the relation of the organs to each other, traceable in some instances to associated malformations, such as absence of the supra-renal capsule, presence of a diaphragmatic hernia, and the like. The main fact made clear by the sectional anatomy was the existence of cervical lordosis and the consequent dislocation of the relation of structures in the neck and thorax.

Before I pass from the morbid anatomy of the anencephalic fœtus I may refer to F. J. Shepherd's article (*Journ. Anat. and Physiol.*, xix. 311, 1885) on the occurrence of the musculus sternalis in this type of monstrosity. It was found in six anencephalics examined, and in three of them it was bilateral. Its association with the teratological state suggested to Shepherd that it might be a rudimentary structure or reversion. The association of anencephaly with the musculus sternalis had been previously pointed out by P. S. Abraham (*Trans. Acad. Med. Ireland*, i. 301, 1883). It is not a constant association.

Associated Malformations.

Anencephaly, being a comparatively common monstrosity, is not infrequently met with in association with other teratological states. I can do little more than name these complications here.

Reference has already been made (p. 335) to the fact that anencephaly may occur in the different forms of double monster. The malformations now to be noticed are in the single fœtus. There may, for instance, be facial fissures of greater or less extent, including hare-lip and cleft palate; three at least of my specimens showed this combination, and in two of these there was adhesion of the amnion (covering the placenta) to the head. There may be cyclopia in some cases (von Lenhossék, *N. Jahrb. d. teutsch. Med. u. Chir.*, iii. 1, 1821; Planchon, *Bull. Soc. anat. de Paris*, xliii. 541, 1868), exomphalos in others (as in three of my forty-six cases), and diaphragmatic hernia with displacement of the abdominal contents into the thoracic cavity in others (as in one of my specimens). Other associated malformations are digital defects (Ballantyne, *Edinb. Med. Journ.*, xl. 1029, 1895), anal imperforation (Perkins, *Med. Rec.*, xlviii. 492, 1895), vascular anomalies, solitary or horse-shoe kidney (Gade, *loc. cit.*), and genital defects such as a rudimentary state of the testicles or ovaries or of the penis (Appert, *Arch. de tocol.*, xxi. 874, 1894). Bifid tongue has been noted (Joly, *France méd.*, xiii. 343, 1866). Club-feet are common, and spina bifida, as has been pointed out, is so common as almost to constitute a part of the malformation. Club-hand is rarer (A. G. Luecke, *Diss. inaug.*, Halis Saxonum, 1854), so is the uterus duplex (J. Klatt, *Diss. inaug.*, Leipzig, 1892), and the cystic liver and kidneys (O. Witzel, *Centrlbl. f. Gynäk.*, iv. 561, 1880).

Teratogenesis.

It is unnecessary to consider at length the various theories of the causation and mode of production of anencephaly. In discussing teratogenesis I constantly had to refer to this monstrosity, for all the theories were made by their proposers to apply to it. Thus we find it explained by means of a maternal impression (p. 112), by injury to the mother (pp. 137, 139, 140), by a fœtal disease such as hydrocephalus (p. 159 *et seq.*), by amniotic (or placental) adhesions (p. 168 *et seq.*), and by arrested development (pp. 206, 216). A few words are all that is necessary on the three last suggestions.

The idea that a fœtal disease such as hydrocephalus is the cause of anencephalus has been popular since the time of Morgagni (E. Mayer, *Amer. Journ. Med. Sc.*, n.s., lxxxiii. 118, 1882; and many others). With the progress of time and the acquirement of further knowledge its terms have been altered; but the notion of a distended condition of the cerebral ventricles preventing the formation of the cranial vault and resulting ultimately in rupture, is in all respects the legitimate modern representative of the old theory. Two great difficulties face the supporters of this view: one is the state of the eyes in anencephalics, for, unless we are to change our ideas of the development of these organs, it is difficult to explain their occasionally perfect formation in association with widespread destruction of the cerebral vesicles, including, of course, the anterior one; the other is the convex curve of the cranial base, for if there has indeed been great intracranial pressure, we should have expected a concavity. If we are to accept this theory we must believe that the destruction of the anterior cerebral vesicle takes place after the outgrowth of the optic evaginations from the telencephalon, and that pressure on the basis cranii is in some way or another abolished; there are manifest difficulties in connection with both. Taruffi (*Storia*, vi. 158, 1891) was inclined to adhere to a pathological theory of origin, but a different one from that referred to above. He saw, in the excessive ossification of the bones of the basis cranii and in the spongy vascular mass occupying the position of the brain, signs of a process analogous to inflammation which had resulted in the production of an erectile tissue (an angiomatous formation arising from the cerebral blood vessels) and in the destruction of the nerve tissues. The difference between the results in anencephaly and in hydrocephalus is due to the effusion being interstitial in the former and interventricular in the latter. I think, however, that it must be admitted that there are grave difficulties in accepting Taruffi's theory of vascular origin for any form other than pseudencephaly. Further, all the theories of fœtal disease as a cause of embryonic monstrosity are to my mind difficult of acceptance, for I believe that the monstrosities arise at a time anterior to the stage of development when diseases, as such, are possible.

It must at the same time be admitted that the strictly embryological theories of anencephaly also contain numerous difficulties. That amniotic attachments and consequent traction upon parts of the head account in part at least for many of the cases of mero-acrania cannot, I think, be doubted. The cases of adhesion of the placental amnion to the deformed cranium are sufficiently numerous to permit us to draw this deduction. Further, the evidence of Comparative Teratology is in favour of this, for all known specimens (there are not many) of anencephaly in the mammalia are instances of mero-acrania, and in some at least of these (p. 188) amniotic bands were present. But this view does not satisfactorily account for the cases of complete anencephaly (holo-acrania) which are the more numerous in the human subject, and which are wholly absent in the other mammals. This negative fact must have a significance: the absence of anencephaly in mammals other than man must have a bearing upon the mode of origin of the monstrosity. I believe its significance has to do with the mode of development of the amnion in the human subject, which, there is reason to maintain, differs from that in the lower animals.

Taking into account all the facts, I am inclined to think that the cases of complete absence of the cranium (holo-acrania) at any rate are arrested developments due to amniotic pressure, while some at least of the cases of partial anencephaly (mero-acrania) are caused by amniotic adhesions (or non-separations), which, while they do not altogether prevent the formation of parts, seriously disturb their normal organogenesis. The arrest in development obviously affects the medullary groove primarily and most markedly, and we may reasonably suppose it to be due to defective formation or separation of the amnion over the cephalic end of the embryo. Some of the differences in the appearances found in different cases may be due to the angle at which the head-end lies at the time when the anomaly is produced (Lebedeff, *Arch. f. path. Anat.*, lxxxvi. 263, 1881); we know that the embryonic axis in its upper part changes its direction during ontogenesis, and in this way different parts of it may fall under the action of amniotic pressure. Further, different effects may be produced by the different dates at which the pressure may cease to act, for it is not maintained that the compressing force continues to act till the end of antenatal life; a certain amount of subsequent development and even of repair may, therefore, follow the teratogenetic epoch and mask the original appearances. The investigation of the early stages of the development of both the human embryo and the human amnion must be awaited before this whole matter can be further elucidated. It is, as I have said, noteworthy that anencephaly is so common in the human subject and so rare in the mammalia generally; it is also very uncommon in birds, and, as Dareste points out, it has very seldom been met with among the results of teratogenetic experiments on the hen's egg (*Production artificielle des monstruosités*, p. 384, Paris, 1891).

Another factor in the teratogenesis of anencephaly which we cannot afford to neglect is the germinal. Direct heredity, of course, is impossible; but the frequency with which family prevalence occurs is most striking; in fact when a woman has once given birth to an anencephalus there is almost a presumption that she will give birth to a second, or at any rate to some other form of monstrosity (Ballantyne, "Recurrent Monstriparity," *Amer. Journ. Obst.*, xli. 577, 1900). This would seem to show that anencephaly may be determined prior to the appearance of the embryo and the amnion; even if this be so, however, it is not to be concluded that the actual formation of the monstrosity is not worked out by amniotic pressure due to amniotic defective development. It may be the amniotic defect which shows the family prevalence.

LITERATURE.

In addition to the references already mentioned in the text (about seventy in number), the following may be named as of special interest; many others are in the *Index Catalogue* and elsewhere :—

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CHAPTER XX

Merosomatous Terata (*cont.*): Malformations of the Cranium. Cephalocele: Definition, Synonyms, Historical Note, Clinical History, Morbid Anatomy, Position, Sac, Foramen, Contents (Hydro-meningocele, Encephalocele, Hydro-encephalocele, Hydro-meningo-encephalocele), Basis Cranii, Associated Malformations, Comparative Teratology, Teratogenesis. Hydrocephalus: Varieties, Definition, Clinical History, Morbid Anatomy, Associated Malformations, Surgical Treatment. Microcephalus: Definition, Historical Note, Clinical History, Morbid Anatomy (Cranium, Brain, Varieties, Other Parts, Associated Malformations), Teratogenesis, Surgical Treatment. Miscellaneous Malformations (Cranial Perforations, Porencephaly, etc.). Omphalocephaly (*Dareste*).

Having in the preceding chapter described in some detail the important monstrosity known as anencephaly, I now proceed to deal with several other malformations of the cranium. The limitations of the available space in a work of this size lead me greatly to curtail the descriptions of them. That the reader may realise this, I may mention that Taruffi in his *Storia della teratologia* gives eighty-eight pages in his sixth volume and sixty-four pages in his eighth to the study of cephaloceles, while I am only able to afford seven or eight pages. There must of necessity be abbreviations; but I shall try to abbreviate by contracting and condensing, not by cutting off and omitting. Under the circumstances, bibliographical references have, with rare exceptions, been sacrificed.

Cephalocele.

Definition.—Consists in the protrusion of part of the cranial contents through a more or less rounded opening in the cranium; the swelling thus produced is covered with skin, altered or unaltered. The chief *synonyms* are "cerebral hernia," "encephalocele," "cranial spina bifida," and "congenital hernia of the head"; the first of these is too closely identified with one theory of origin, the second is better reserved for the naming of a variety, the third is awkward, and the fourth is too long. "Cephalocele," proposed by W. Heineke, is the best general term.

Frequency.—It is comparatively rare; three cases only occurred in 12,900 labours (Trélat); and in my series of 325 specimens of antenatal disease and deformity there were only eight instances of cephalocele in contrast with forty-six of anencephaly, but, of course, the discrepancy may be due to other reasons than comparative rarity.

Historical Notes.—First reported instance by Forestus (1590); few cases in seventeenth century, and curious errors as to their nature ("penis at root of nose," "scrotum at back of head," etc.); first illuminating monograph by J. F. C. Corvinus (*Diss. inaug.*, Argentorati) in 1749; since then, a long series of articles (clinical, pathological, statistical, pathogenetic, and therapeutic) by C. F. F. Buettner in 1832, by A. Spring in 1854 (a long and learned monograph of 150 pages, very worthy of consultation, but not often consulted, in the original at least, in these days), by J. Z. Laurence in 1856 (good tabular analysis), by G. Reali in 1874 (in a *Dissertation* of Zürich, which Taruffi (mirabile dictu!) had not seen in the original), by C. Taruffi himself in 1873 and 1891, by T. Ackermann in 1882, by P. Berger in 1890 and in 1891, and by G. Muscatello in 1894.

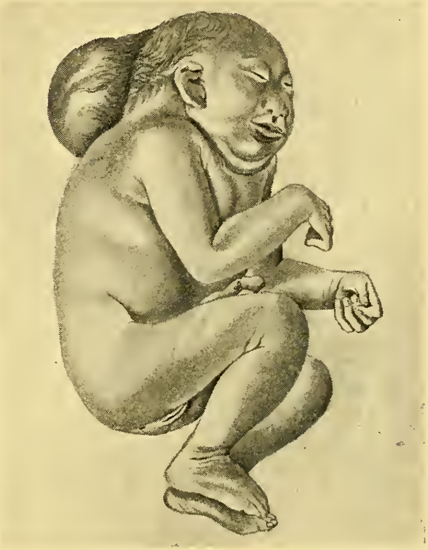


Fig. 59.—Occipital Encephalocele. Specimen No. 26.

Clinical History.—Of the antenatal clinical history of fœtuses with cephaloceles little is known. One of my cases, however, had an interesting record, which I give here briefly. This specimen (Fig. 59) I received from Dr. A. A. Martin of North Shields in 1890. It was born at the seventh month; the head or rather the occipital encephalocelic sac presented; on the rupture of the membranes there was a tremendous gush of waters, for there was marked hydramnios. The pains were feeble; forceps extraction; partially retained placenta. The fœtus, a female, never breathed. This was the mother's fourth child; her first, born at the eighth month, was "exactly similar"; her second and third were born at

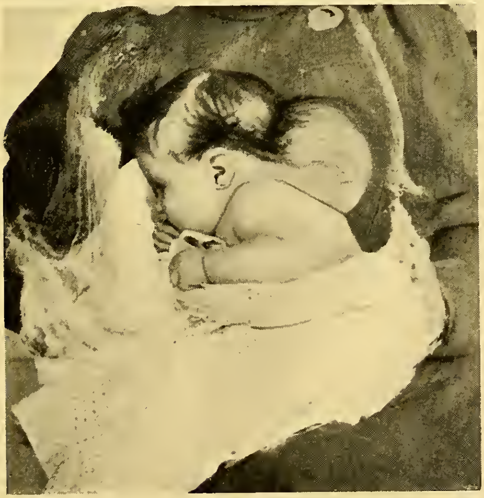


Fig. 60.—Dr. Charles's Case of Occipital Encephalocele with Accessory Brain.

full time, and are alive and healthy; with all the four labours there was hydramnios. Three clinical facts emerge from this history, namely, premature termination of gestation, coexistence of hydramnios, and family prevalence.

Another interesting history was communicated to me by Dr. Etta Charles of Summitville, Indiana, U.S.A., who sent me notes and photographs. The mother, who was about thirty-two years old, and had two living female children (ages fifteen and thirteen years), gave birth in 1897 to a girl baby (Fig. 60) with an encephalocele arising from the lower part of the occiput and involving the foramen magnum and upper cervical vertebræ. I shall have occasion to refer again to the morbid anatomy of this case; but it may be added that after several operations the child died. Some eight months later the mother was operated upon for abdominal tumour, and an ovarian cyst weighing 35 lbs. was removed; at the operation the uterus was found to be two months pregnant. The pregnancy went on and the patient greatly feared she might give birth to another monstrosity. Labour came on about the sixth month; there was hydramnios; an anencephalic (pseudencephalic) female fœtus was born; and a post-mortem examination revealed transposition of the thoraco-abdominal organs (heart, liver), and other anomalies. In the former pregnancy the mother was in good spirits and had no fears; in the latter she lived in terror that she might give birth to another monster.

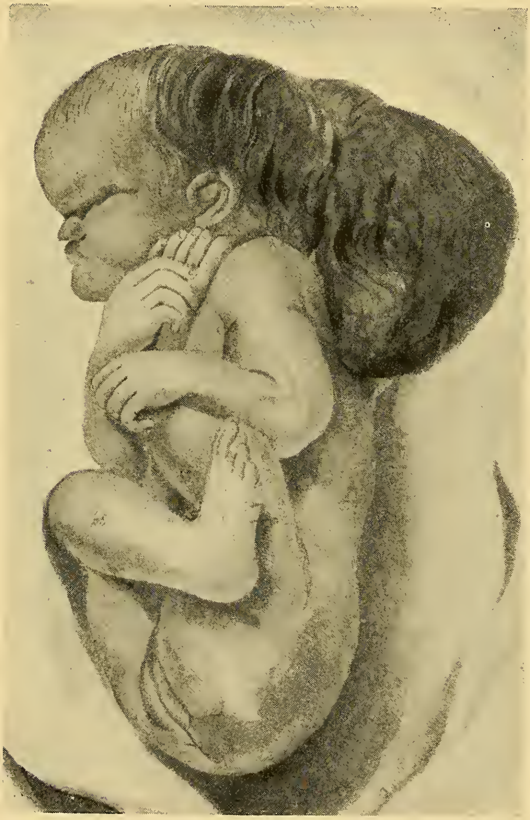


Fig. 61.—Occipital Encephalocele. Specimen No. 22.

In one of Vannoni's cases (1850–51) a woman gave birth, first, to an infant with an occipital encephalocele, and her next pregnancy ended in the birth of one with a cephalocele of the vertex (left parietal region); in another of his cases the mother suffered violence during pregnancy. Twin brothers affected with occipital cephalocele were seen by Meckel (1822), and Carli (1863) relates the story of a woman who gave birth to two anencephalic fœtuses in her first two pregnancies and to an infant with a cephalocele in her third. It may, therefore, be concluded that the history of the pregnancy that ends in the birth of an infant with a cephalocele resembles in several characters that which is accompanied by anencephaly.

The postnatal clinical history of the deformed infant differs in many respects from that of the anencephalic fœtus. The child may not only survive birth, but may live for weeks, months, or even years; and the malformation may even spontaneously disappear. When, however, the cephalocele is large, life is usually measured by weeks, and the cause of death is inflammation due to traumatism or operative interference. The small cephaloceles, on the other hand, may be met with in adults (cases at seventeen, twenty, twenty-three, thirty-three, and even at fifty-eight years having been reported); the hydro-meningoceles are less fatal than the encephaloceles and yield slightly better results if operated upon (by compression, ligature, or, best, by excision). Of my eight cases, four died at birth; three lived for some weeks; and one (a fronto-nasal cephalocele of small size) was five months old when seen by me. Two died after operation; but in one of these cases excision was performed only for cosmetic purposes and not with the hope of cure.

Infants with large cephaloceles are usually born with difficulty. The diagnosis is not generally made before labour, or, indeed, till the os is fully dilated, and even then they are generally mistaken for cases of hydrocephalus and treated as if they were such. After birth they may in certain cases require to be diagnosed from dermoids and serous cysts, from cephalhæmatomata, and from intranatal hernias.

Morbid Anatomy.

In considering the morbid anatomy of this monstrosity I shall take up (1) the position of the cephalocele, (2) the sac and the opening through which it protrudes, (3) the contents, including the varieties founded upon the nature of the contents, (4) the state of the rest of the cranium, and (5) the associated malformations.

(1) *Position of the Cephalocele.*—Most commonly it is in posterior part of cranium (occipital), when it may be (1) in middle line below occipital protuberance, or above it (in position of ossicle of Kerckring), or at posterior fontanelle; or (2) lateral, at postero-lateral fontanelle, or in the lambdoidal suture. The commonest of all is the first, and then the opening may extend to the foramen magnum and even to the cervical vertebræ. Next in frequency, it is in the anterior part of cranium (sincipital), when it may be (1) in the middle line, in the naso-frontal, in the frontal, or in the naso-ethmoidal sutures; or (2) lateral, between the nasal process of the superior maxilla and the lachrymal bone, or supra-orbital, or at the outer angle of the orbit. Less often it is in the part of the cranial vault known as the vertex, when it may be (1) lateral, in the parietal or temporal bones (right

or left) or in the coronal suture (right or left half); or (2) median, in the anterior fontanelle or in the sagittal suture. Rarest of all it is in the base of the cranium, when, again, it may be (1) median, in the sella turcica or between the sphenoid and ethmoid; or (2) lateral, at the sphenoidal or spheno-maxillary fissures. Save in cephaloceles of the vertex of the cranium, the opening is more frequently in the middle line than at the sides; more often at the posterior and anterior ends of the middle line than midway, more often at the posterior than at the anterior end; and when it is at the posterior end it is more often below than above the occipital protuberance.

(2) *The Sac of the Cephalocele and the Opening in the Cranium.*—The sac varies (1) in size, from that of a pea to that of a fœtal head or larger; (2) in shape, being spherical, elliptical, pear-shaped, or cylindrical, with one or two or (rarely) more lobes, and with or without a pedicle; (3) in its consistence, being cystic or soft and doughy in accordance with its contents; (4) in its coverings, which may be unaltered skin, aponeurosis, and cerebral membranes, or (more often) modified skin (hairless save at margins, red, thick or thin, vascular) and modified cerebral membranes (no dura; thickened arachnoid and pia, often in a myxomatous state). Sometimes the coverings show cicatrices or amniotic filaments or fringes passing to placenta; such specimens are not far removed from instances of mero-acrania, in fact there is no clear dividing line. The sac may be reducible by pressure, non-reducible, or partially reducible (depending largely on the nature of its contents); when reduced, strabismus, convulsions, and coma may follow. The sac may pulsate synchronously with the pulse or the respiration. The orifice through which the sac protrudes has usually smooth osseous (rarely membranous) margins, exceptionally they are irregular; it is round or oval, small or large, but never large enough to allow escape of whole brain or even of a hemisphere.

(3) *The Contents of the Cephalocele.*—According to their contents, cephaloceles may be arranged in four groups (*vide infra*):

(*a*) Hydro-meningocele or Meningocele: consists of a protrusion of the cerebral membranes (usually altered), containing fluid only; gives fluctuation, is transparent, and can be diminished by compression; sometimes its cavity does not communicate with interior of cranium; is situated usually posteriorly (occipital), less commonly at vertex, rarely anteriorly (sincipital); and is a comparatively rare form of cephalocele (16 to 20 per cent.). It may be pedunculated, and may or may not communicate with an enlarged cerebral ventricle; and Bland-Sutton (*Tumours*, p. 516, 1903) regards an occipital meningocele as an expanded fourth ventricle or as "hydrocephalus limited to the fourth ventricle," and thinks the cerebellum is entirely absent and that the flocculus is enlarged.

(*b*) Encephalocele: consists in a protrusion from cranium of part of cerebrum or cerebellum; is the most common of all the cephaloceles (54 per cent.); has soft, doughy consistence, is opaque, is little or not at all reducible by compression, and when pressed upon causes convulsions or syncope; it pulsates synchronously with the pulse; is more common posteriorly (occipital), but is not infrequent anteriorly (sincipital), rare at the vertex; and it may be associated with distension of the cerebral ventricles inside the cranium. Its contents, when it is posterior, may be cerebellum alone or with one or both occipital lobes of cerebrum, or one or both occipital lobes without cerebellum, or unrecognisable part of brain (a neoplasm); when anterior or at vertex the contents are the cerebral lobes which correspond to the position of the opening, or an unrecognisable mass of brain tissue (a neoplasm or cephaloma).

(*c*) Hydro-encephalocele or Hydrencephalocele: consists in a protrusion of brain substance which contains in its interior a cystic cavity full of fluid; has characters resembling in some cases those of the hydro-meningocele, and in others those of the encephalocele, or partaking of both; occupies the same positions as the encephaloceles, and in much the same order of frequency; is a rarer form than either encephalocele or hydro-meningocele (11 per cent.); and in its structure it is said to resemble hydrocephalus when there is no protrusion, the brain substance being possibly reduced to a very thin external layer.

(*d*) Hydro-meningo-encephalocele: consists in the protrusion of brain substance, along with the presence of fluid between the membranes external to the cerebral protrusion; is the rarest of all the cephaloceles (9·8 per cent.); it may be situated posteriorly, anteriorly, or at the vertex, but most often posteriorly (although number of cases is too small to give value to statistics); and it may contain various lobes of the cerebrum and (when occipital) of the cerebellum.

With regard to the contents in general, it may be added that in all the varieties which contain cerebral substance the part so contained may apparently be of the nature of an accessory production. In Dr. Etta Charles's case, to which I have already referred, the cerebrum and cerebellum inside the cranium were apparently normal and intact, while lying in the sac was an accessory brain (cerebrum and cerebellum) engrafted on the cord near the medulla and of the size of a small orange. Something of the same kind was detected at the incomplete autopsy on a case of large occipital encephalocele which I saw in connection with the Cowgate Dispensary in 1895 (Specimen No. 143); the child, a male, died on the eighth day, and the contents of the sac seemed to represent accessory structures.

(4) *The Vault and Basis Cranii.*—The rest of the head may or may not be greatly altered in cases of cephalocele. In the instances of cephalocele in the anterior part of the cranial vault, the head may not be altered at all save when hydrocephalus exists as a complication; when the protrusion is at the vertex the alteration is not great, being generally a depression of the bones due possibly to the weight of the extra-cranial portion; but when the cephalocele is posterior the shape of the rest of the head may be markedly abnormal. Even in the occipital cases, however, the deformity is not necessarily great if the cephalocele be below the occipital protuberance and be of the nature of a hydro-meningocele. When the cephalocele is in the

upper part of the supra-occiput, and when it affects the posterior fontanelle, and when the occipital lobes enter into its composition, then the head is much modified: it is of small size, the bones are close together, the middle part of the vault is saddle-shaped (clinocephalus), there is cyphosis at the sphenoidal angle at the basis cranii, prognathism, and elongation of the nasal and superior maxillary bones. The cyphosis of the basis cranii is a very striking character, and there may actually be a dislocation between the basi-occiput and the post-sphenoid. It will be remembered that these changes occurred also in anencephaly (p. 342). When, however, hydrocephalus exists, the whole head is enlarged and the sphenoidal angle is enlarged, and hyper-orthognathism takes the place of prognathism. Many very interesting but not altogether satisfactory explanations have been given of these architectonic alterations in the cranium; in all of them too much attention is paid to the relation of parts as they exist at birth and too little to what was the state of matters in the early period when the monstrosity was produced.

It may be noted, here, that the supra-renal capsules and sympathetic system have been found to be normal in cephalocele; this is interesting in relation to their state in anencephaly.

(5) *Associated Malformations.*—Like all monstrosities, cephaloceles may be associated with other malformations, among which may be named spina bifida, hydrocephalus, hare-lip, cleft palate, club-foot, umbilical hernia, exomphalos, ectopia vesicæ, cyclopia, transposition of the viscera, cystic kidney, amniotic adhesions and bands, and so-called congenital rickets. In a cephalocele of the occipital region below the level of the protuberance, cervical spina bifida is so commonly associated as to be almost an integral part of the teratological state. Hydrocephalus, also, exists with great frequency.

(6) *Comparative Teratology.*—Like anencephaly, cephalocele is a very rare malformation among the lower animals. When it does occur, as in the calf, the lamb, the pig, the kitten, the puppy, or the foal, it is most often found at the frontal end of the cranium. It may be associated with amniotic adhesions. It may, however, be met with more frequently in birds than in mammals, and may in them be the distinctive character of a variety or race as well as a sporadic malformation; this subject has been dealt with by Darwin, Virchow, and several others, and constitutes an interesting chapter in Comparative Teratology.

Teratogenesis.

A great amount of ingenuity has been almost wasted over attempts to explain the origin and mode of production of cases of cephalocele, and that for a reason which will be explained immediately. Let me, first, very briefly indicate some of the theories. Placing on one side the theories of external or internal maternal traumatism and diseased states (alcoholism, etc.) of the parents, I may state, as follow, the alleged causes in the different varieties of cephalocele.

In cases of hydro-meningocele, dropsical distension of the cerebral ventricles, and a localised inflammation of the cerebral membranes (with accumulation of serum) are views that have been entertained; but as neither of these states may exist, such views fall to the ground as insufficient. In the combination of cranial meningocele with encephalocele (hydro-meningo-encephalocele), it has been assumed that a localised meningitis exists first, and by weakening the cranium prepares the way for the escape of the cerebrum; but apart from other difficulties, there is the fact that solid encephaloceles may be met with.

Round the causation of encephalocele the greatest controversy has taken place. It has been ascribed to smallness of the cranial cavity due to synostosis, a fact which fails to explain encephalocele when it occurs in a membranous cranium. It has, on the other hand, been attributed to defective ossification of certain areas of the cranial vault; but as every one knows, such spaces may exist without any encephalocele. It has also been assigned to increased intracranial pressure, which in its turn has been ascribed to ventricular distension (hydrocephalus), to cerebral hypertrophy (for in many instances there is no enlargement of ventricles), or to œdematous swelling of the brain. Finally, hydro-encephalocele has been confidently attributed to localised accumulation of fluid in one or other of the cerebral ventricles or in a part of one of the ventricles.

Now, in all these theories, it will be observed that it is assumed that the malformation supervenes upon a normal condition, and even upon a normal condition of a fully formed structure. It is taken for granted that there is first of all a cranium (already ossified) containing a brain (developed up to the degree existing at birth); that then a pathological process of the nature of a disease attacks the parts, enlarges some structures, weakens others; and that, finally, enlarged organs push their way through weakened containing structures and so produce a cephalocele. In other words, it is thought that the malformation arises in the fœtal period and as the result of a fœtal disease. If this ever occur, it must, I think, be rare. More reasonable is it to regard all the morbid states found (enlarged part, dropsical distension, deficient ossification, etc.) as parts of the malformation, not as causes leading to it. It is absolutely necessary to form a visual image of the head during its embryological development and not after it is formed, and then to try to picture to one's self its maldevelopment. We must not think of intracranial parts being pushed out at cranial apertures and so becoming extracranial; we must imagine parts of the anlage of the brain (*e.g.* the cerebral vesicles and undifferentiated membranes) lying originally outside what is to be the cranium and developing in their ectopic position. In support of this theory is the fact that occasionally an accessory cerebral structure is found in the cephalocele; that structure, it is reasonable to suppose, was originally outside the anlage of the nervous system although attached to it. If it be asked, what is the cause of the accessory part, we, of course, have no satisfactory answer; but the idea of a purely germinal (pre-embryonic) factor suggests itself. To sum up; it is not claimed that the embryological theory explains all the facts, but it explains them better than the pathological hypothesis, and with an extension of our knowledge of ontogenesis and an acquaintance with the laws of germinal pathology it may yet be found to be sufficient. The combination of the idea of an arrested embryonic development and excessive germinal activity seems to me to contain the explanation.

Hydrocephalus.

In the first section of this MANUAL I referred to hydrocephalus, and I again take notice of it here. The reason is not far to seek. There are two theories of the origin and nature of hydrocephalus: one regards it as a fœtal disease, and on this account it found a place in Volume I.; the other looks upon it as an embryonic malformation, and so it appears in the present chapter. It is probably more correct to say that there are two varieties of antenatal hydrocephalus, a pathological (or nosological) and a teratological; at any rate such is the current belief at the present time. I prefer, however, to state the matter somewhat differently: I believe that antenatal hydrocephalus is generally due to an embryological arrest of development to which may be superadded in the fœtal period a disease affecting the malformed parts, but I admit the possibility of hydrocephalus arising, without a preceding malformation, in the fœtal epoch from a disease, just as it sometimes originates in postnatal life.

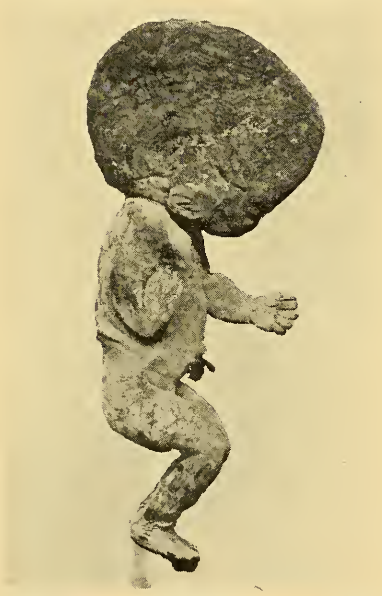
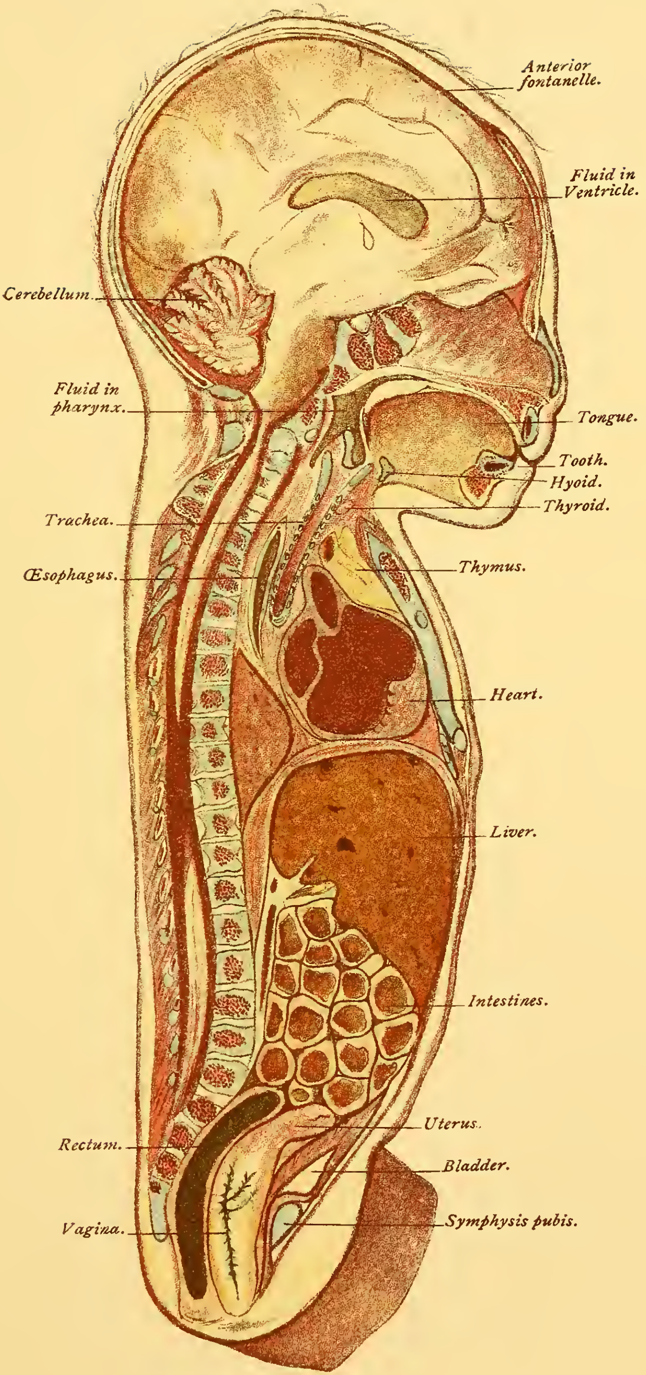


FIG. 62.—Case of Hydrocephalus with Deformity of Right Arm and Hand (Absence of Thumb). Specimen No. 71.

The condition itself is well known to the obstetrician, the pediatrist, and the surgeon. It consists essentially in the presence of a fluid accumulation inside the cranium, generally within the distended cerebral ventricles and their communicating passages, but occasionally between the membranes.

It is sometimes, but apparently not very often, associated with hydramnios in pregnancy; there may also be oligohydramnion (Bonnaire, *Arch. de tocol.*, xxi. 157, 1894). Its diagnosis is rarely made till labour is in progress, when the large size of the head, the width of its sutures and fontanelles, and the parchment-like consistence of the vault bones will lead to recognition. It is most

PLATE XIX.


Anterior fontanelle.
Fluid in Ventricle.
Cerebellum.
Fluid in pharynx.
Tongue.
Tooth.
Hyoid.
Thyroid.
Trachea.
Œsophagus.
Thymus.
Heart.
Liver.
Intestines.
Uterus.
Rectum.
Bladder.
Symphysis pubis.
Vagina.

likely to be confounded with a cranial meningocele or encephalocele or with a large sacral cyst. In breech cases, when the breech has been born and a lumbo-sacral spina bifida appears, the chances are that a hydrocephalic head is to follow. If unrecognised, hydrocephalus may prove a serious complication of labour.

The reproductive history of the mother is sometimes interesting. Family prevalence may be met with, several hydrocephalic infants being born to the same parents. More interesting still are the records in which hydrocephalus and other malformations have followed one another in the same family history. For instance, one of my specimens of hydrocephalus (Fig. 62) was born to a woman who afterwards had an anencephalic fœtus, and, later still, one with malformation of thumbs, absence of radii, and commencing hydrocephalus; all the three fœtuses had deformities of the thumbs, and the mother, her sister, and her mother had defective thumb muscles. A frozen section of the third fœtus is shown in Plate XIX., and it will be noted that there is commencing hydrocephalus although no external indications of it were present. In connection with one of my specimens of iniencephaly (No. 155) the mother had in a previous pregnancy had a hydrocephalic child.

Consanguinity of the parents does not appear to be specially associated with hydrocephalus in the offspring; but parental syphilis seems to be so frequently met with as to suggest more than a casual coincidence. E. Fournier (*Stigmates dystrophiques de l'hérédo-syphilis*, p. 66, 1898) has indeed collected together from literature as many as 170 cases in which hydrocephalus occurred in fœtuses and infants who were the subjects of hereditary syphilis. Tubercle, nervous diseases, and alcoholism in the parents have also been blamed.

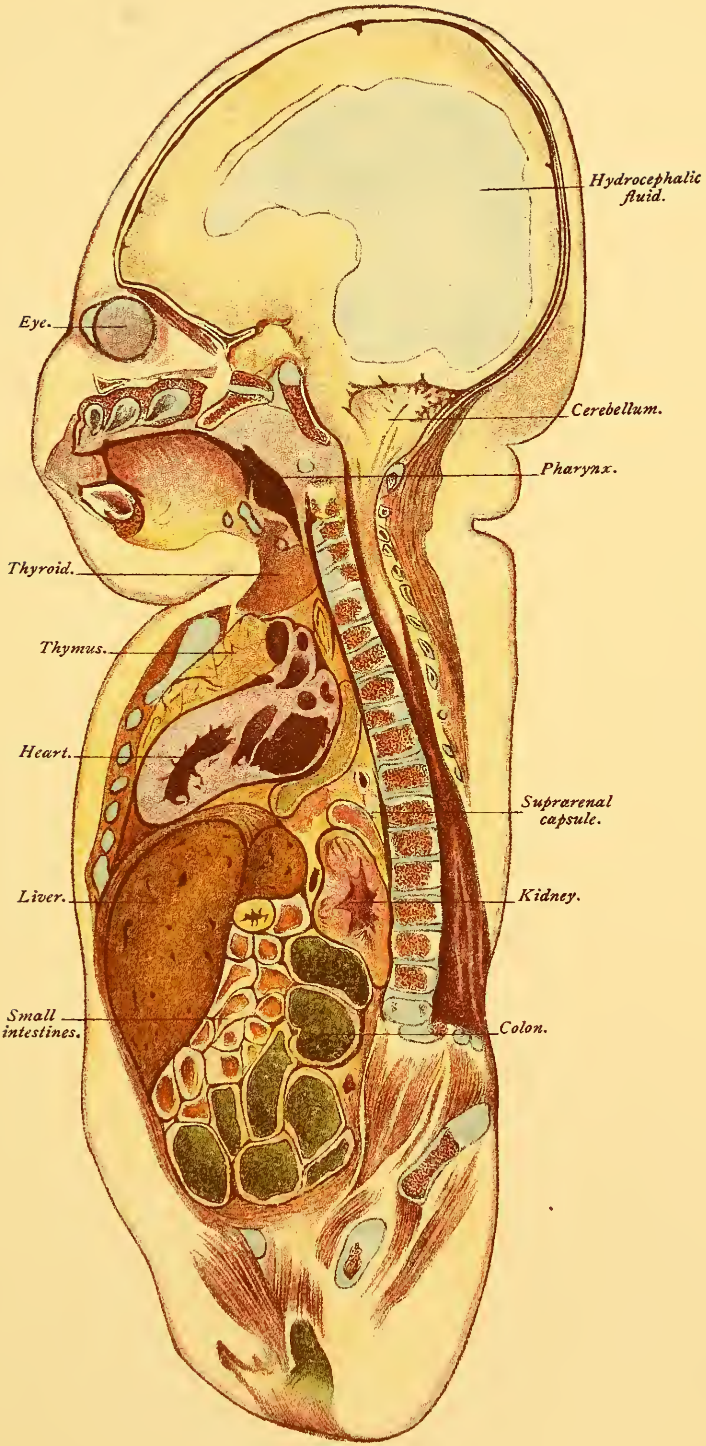
The morbid anatomy of hydrocephalus has only been worked out within recent years, its finer details having been specially investigated by H. Virchow (*Fest-Schr. Albert v. Kölliker*, p. 305, 1887), H. Chiari (*Über Veränderungen des Kleinhirns . . . in Folge von congenitaler Hydrocephalie des Grosshirns*, Wien, 1895), and by M. Karch (*Diss. inaug.*, Würzburg, 1898). As a general rule, the head is greatly enlarged in all its diameters, and the great round cranium contrasts in a very striking fashion with the small triangular face; the sutures and fontanelles are wide, and in some cases there are little more than small islands of bone in a sea of membrane. In rare cases there is not largeness but smallness of the hydrocephalic head. I found, for instance, in an autopsy which I performed for Dr. Berry Hart on an infant that died in the Edinburgh Royal Maternity Hospital in March 1895, that although the head was small (so small that the baby had been known as "The Monkey" in the Hospital) yet the contents above the tentorium cerebelli were solely fluid; the infant had, nevertheless, lived for nine days, and had differed from other babies only in not opening its eyes and in not sucking properly. It was cyanosed when born and remained so. It kept constantly moving its tongue backwards and forwards. The mother was a I-para, and the labour was at the full term. The child weighed 5 lbs.; the occipito-mental circumference of the head was 13¼ inches and the occipito-frontal 11½ inches. The foramen ovale in the heart was patent, and the anterior fontanelle nearly closed. Cases of this kind belong to the group of the micro-hydrocephalics; a somewhat similar case was described by S. De Sanctis in 1900 (*Ann. di neurol.*, xviii. 265, 361, 1900). In a third group of cases are the infants in whom the head at birth is normal in size, and in whom, after an apparent latent period, hydrocephalic enlargement appears. Such cases are figured in Plates XVIII., XIX., and XX.; in all of them hydrocephalus was not suspected before the sections were made.

The essential character of hydrocephalus, therefore, is not found in the size of the head but in the dilated condition of the cerebral ventricles. Liquid in excess is usually found in all the ventricles (especially in the lateral, but also in the third, and sometimes in the fourth); it is commonly equal on both sides; the foramina of Monro and the aqueduct of Sylvius are distended; and the liquid itself has the characters of cerebro-spinal fluid, or may contain much albumen. It is not always that a communication (foramen of Majendie) between the fourth ventricle and the sub-arachnoid space can be demonstrated (J. O'Carroll, *Trans. R. Acad. Med. Ireland*, xii. 293, 1894). In some instances the cerebrum may be practically absent, some traces only of it being found on the basis cranii; in other cases the malformation is less pronounced and the walls of the hemispheres may be thinned, and the fissure of Sylvius may be widely open exposing the island of Reil. The corpus callosum, trigone, and septum lucidum may be absent. The dilatation is chiefly at the expense of the medullary part of the cerebrum, and the cortex may be comparatively little altered. The ventricular membrane may be thickened, and the choroid plexus may be variously altered (hypertrophic, flattened, anæmic).

The changes in the cerebellum have been worked out by H. Chiari and others. It may be normal; on the other hand, it may be absent, atrophic, asymmetrical, or hypertrophic. Further, a curious change in its form may be found: there may be an elongation of the tonsils and of the median part of the inferior lobe, and these may descend into the spinal canal (Plate XVIII.). The fourth ventricle, also, may be displaced downwards. Chiari has arranged these cerebellar and associated changes in four types with subdivisions, and to his work (*op. cit.*) the reader is referred for full details. The falx cerebri and tentorium cerebelli may be absent. There commonly is great obliquity and shortness of the basilar groove and enlargement of the foramen magnum; the floor of the orbital cavity is usually lowered, giving to the eyes their peculiar appearance. The optic chiasma may be wanting (H. B. Ferris, *Yale Med. Journ.*, i. 239, 1895). The spinal cord may be found intact, but sometimes there is hydromyelia, especially if spina bifida coexist.

Associated malformations are common and interesting. Among the more frequent may be named spina bifida, cephalocele, and club-feet. Hare-lip and cleft palate are also frequent. Among the less common are facial fissures (as in A. Heinicke's case, *Diss. inaug.*, Königsberg i. Pr., 1890), defective external ears and polydactyly

PLATE XX


Hydrocephalic fluid.
Eye.
Cerebellum.
Pharynx.
Thyroid.
Thymus.
Heart.
Suprarenal capsule.
Liver.
Kidney.
Small intestines.
Colon.

with facial fissures (as in L. Hirschberg's specimen, *Diss. inaug.*, Königsberg i. Pr., 1891), exomphalos (as in O. Schmidt's case, *Diss. inaug.*, Berlin, 1885), and absence of the nose and one eye (in one of E. Wernicke's specimens, *Diss. inaug.*, Berlin, 1885). I have examined seven cases: in two there were digital defects, in two spina bifida, in several the feet were clubbed, and in one there was cyclopia and absence of the lower jaw. The association of cyclopia with hydrocephalus is well exhibited in a female fœtus figured and described by Beveridge (*Northumb. and Durham Med. Journ.*, ii. 51, 1894). It is also met with in cases of so-called fœtal rickets and phocomely. In some instances of hydrocephalus the fluid accumulation may be localised, and then an irregularly shaped head may result; if, for instance, there is premature synostosis of the sagittal suture, scaphocephaly will follow.

Great activity has been shown of recent years in the surgical treatment of hydrocephalus, but as yet without conspicuous success. At present most attempts aim not at cure but at cosmetic effects. To quote from H. J. Stiles' article (*Brit. Med. Journ.*, ii. for 1902, p. 673): "Repeated tapping (with or without compression of the head), intermittent or continued capillary drainage of the lateral ventricles, drainage into the loose cellular area beneath the occipito-frontalis (Mikulicz), intermittent and continuous lumbar drainage, capillary drainage into the sub-arachnoid space (Sutherland and Watson Cheyne), injection of Morton's fluid, repeated and more or less complete evacuation of the fluid by tapping and simultaneous introduction of aseptic air (Ewart and Dickinson), and drainage from the spinal canal into the peritoneal cavity, have all been tried, with, I fear, it must be admitted, only partial and temporary success." Stiles himself tried the last-named method, and led some strands of horsehair from the sub-dural space in the lumbar region into the peritoneal cavity just external to the descending colon; but without success. Probably, in the meantime, the surgeon's efforts will be best restricted to endeavouring to diminish the great bulk of the head, and so lessen the distress of the child's parents.

Microcephaly.

The microcephalous individual is one whose head and brain are abnormally small. Attempts have been made to fix the limits of cranial size or capacity within which microcephaly lies; but it is impossible thus to define the anomaly, for such measurements must vary with the age of the patient and the dimensions of the body, and for the additional reason that it is the condition of the brain rather than of the containing cavity which determines the morbid state.

Very few cases have been described as they exist at or soon after birth; for the malformation does not interfere with postnatal life of a vegetative kind, and it is, therefore, not till some months have elapsed that it is noticed that the child is mentally deficient. In C. Giacomini's fine monograph (*Cervelli dei microcefali*, Torino, 1890), which every one who is specially interested in microcephaly ought to study, there was only one observation out of nineteen on a new-born infant. The condition is truly antenatal, but it is, as I have said, rare for it to be studied until antenatal life has been left months or years behind.

Such cases have always created great interest. In olden times (and in popular opinion now-a-days) they were regarded with a strange mixture of curiosity and disgust as ape-men ("hommes-singes"); and in recent times they have formed the foundation of many theories regarding the descent (or ascent) of man from simian ancestors. It appears to me, however, that the right way to look upon microcephaly is as an antenatal arrest of growth and development; as such it proves no more in respect to the primal origin of man than does anencephaly or exomphalos. From antiquarian observations it would seem to have been observed and recorded far back in the world's history.

Little is known of the antenatal clinical history of the microcephalic fœtuses, for, as I have said, interest in them is not often excited till some months after birth. At the same time it would appear that hydramnios is not an uncommon occurrence, and that family prevalence is frequent. Two microcephalics have been born to the same mother, as in Giacomini's first case (in which the birth of the second defective child was ascribed to a maternal impression received from the first); three microcephalic brothers have been met with (J. V. Laborde, *Rev. scient.*, 4 s., iii. 579, 1895); four microcephalics and a clinocephalic occurred in the same family (S. N. Tirrizzi, *Atti d. Accad. Gioenia di sc. nat. in Catania*, 3 s., xv. 1, 1881); and in the famous Becker family there were five individuals affected with microcephaly (O. Flesch, *Verhandl. d. Berl. Gesellsch. f. Anthrop.*, 72, 1883; T. L. W. Bischoff, *Anatomisches Beschreibung eines mikrocephalen 8 jährigen Mädchens, Helene Becker aus Offenbach*, München, 1873; N. Rüdinger, *Sitzungsb. d. math.-phys. Cl. d. k.-bayer. Akad. d. Wissensch. z. München*, xv. 112, 1885; Stendel, *Med. Cor.-Bl. d. Württemb. ärztl. Ver.*, lvi. 33, 1886; and others). The so-called Aztec man and woman (Indians from Mexico), exhibited in various parts of the world, were instances of microcephaly; they were married in 1867, but had no offspring (F. Birkner, *Arch. f. Anthrop.*, xxv. 45, 1898). It has been affirmed that in one instance only has a microcephalic woman conceived, and that in her case the fœtus was born dead (Ireland, in Hack Tuke's *Dictionary of Psychological Medicine*, ii. 807, 1892). One of Shuttleworth's patients (*Journ. Ment. Sc.*, xxiv. 438, 1878) had consanguineous parents; and the parents' late marriage (*opsigamy*, as it is called) has been alleged to be a causal factor. The family history in Frey's case (*Arch. f. Anthrop.*, xxv. 33, 1898) was interesting; there was first a normal boy, then a microcephalous boy, then triplets (a normal boy, and a microcephalous boy and girl), then a microcephalous girl, and finally two normal children. Into the matter of the other functions of the body and mind in this form of malformation it is not my purpose to enter; it lies outside the sphere of antenatal pathology, although, of course, it very evidently falls within that of the postponed effects of antenatal pathology.

The *morbid anatomy* of microcephaly raises several interesting problems. I shall, as usual, consider (1) the cranium, (2) its contents, (3) other parts of the nervous system, and (4) associated malformations.

(1) At birth the *cranium* may show premature closure of one or more of the sutures; but, as this is not a constant character, it follows that the theory of microcephaly being produced by this untimely synostosis cannot be maintained. The cranium is small in all its parts and diameters, but especially in the frontal region; the occipital region is more expanded, and the occipital condyles are prominent. The head has, therefore, a peculiar avian character, which has earned for the malformation such names as "homme-oiseau" and "Vogel-Kopf." There is prognathism of the face; the basis cranii is contracted, although not so markedly as the vault; the ethmoidal fossa is deep and narrow. Other characters, including the state of the temporal ridges, mastoid processes, external auditory meatus, etc. etc., will be found described in such monographs as those of Cunningham and Telford-Smith (*Trans. Roy. Soc. Dublin*, 2 s., v. 287, 1895), and of Sir George Humphry (*Journ. Anat. and Physiol.*, xxix. 304, 1895). It may be added that there is nothing in the anatomy of the parts to support the idea that the defective development of the brain is due to cranial compression; there are, on the other hand, certain characters which may be called "simian," although it does not, of necessity, follow that their presence demonstrates the atavistic origin of microcephaly.

(2) The *brain*, which lies within the microcephalic cranium, is also small in size; there is microencephaly as well as microcephaly. Indeed there is every reason to regard the smallness of the brain as the primary condition, and that of the cranium as secondary to it. The weight of the brain has varied from less than an ounce (40 grms.) and nearly 4 oz. (107 grms.) in the new-born infant to a little more than 2 lbs. in an adult (Giacomini). A brain weighing only 7 oz. from a girl aged twelve years was shown (by Fletcher Beach) to Ireland.

The subject of the characters of the brain in microcephaly is a complicated one, but Giacomini (*op. cit.*) and others have done much to remove some of the confusion. Giacomini, especially, by arranging the recorded cases in groups, has thrown some light into this dark corner of antenatal pathology. He has pointed out that there is no typical brain of microcephaly, none which constitutes a constant and characteristic type; there are only microcephalic brains. These cannot be satisfactorily arranged in groups either according to weight, or to volume, or to the capacity of the crania containing them; it is necessary to take into account other characters. Giacomini divides all the cases into two large groups: one contains the true microcephalics and the other the pseudo-microcephalics. He prefers the words microencephaly and pseudo-microencephaly, but the distinction is comparatively unimportant. He has also a third group in which other malformations are present as well as microcephaly; the members of this division he does not regard as microcephalics proper. I think, however, that Giacomini is too insistent upon a clear dividing line; I prefer to regard these cases as instances of microcephaly with associated malformations, and I consider his pseudo-microcephalics as cases of microcephaly with associated morbid processes of the nature of fœtal or infantile disease. Whether microcephaly occurs alone or is associated with fœtal disease or embryonic malformation depends, to my thinking, upon the time when the morbid cause comes into action, and how long it continues to act. If the reader has read the chapters on Teratogenesis he will understand what I mean. True microcephaly, as Giacomini considers it, is apparently an arrested development of the central nervous system at a comparatively late date in antenatal life; such an arrest is possible because the brain is slow in passing out of the embryonic into the fœtal state, indeed it is still in the embryonic condition when most of the other systems are in the fœtal. Hence it comes about that we may meet with microcephaly alone with no other malformations of brain or other part. In such cases I hold that the causal factor (whatever it was) came into play late in antenatal life when the other parts were already formed. In other instances diseases of neighbouring structures, of the brain itself, are discovered (Giacomini's pseudo-microcephalics); these I regard as the results of the same cause; but that cause is acting on structures no longer in the formative phase, and so diseases not malformations are produced. In yet other cases there are coexistent malformations of the brain or of more distant parts: those of the brain are more fundamental than the slight deviations which Giacomini allows as characters of microcephaly, and they may be supposed to have been produced by a cause acting earlier, when the brain had not assumed its final form and parts; those of more distant parts are obviously the result of the action of a cause at a still earlier date in antenatal life, when other parts of the body than the nervous system were still in the embryonic or formative stage. From this standpoint let us now look at the cerebral conditions in microcephaly.

The brain is simple, poor in convolutions, and those that are present are coarse and lacking in complexity (microgyry); the secondary and tertiary fissures are wanting, as are also bridging convolutions. The brain, then, is, in these cases, the human brain in miniature; and we may imagine an arrest near the end of antenatal life or even later. In another group of instances of microcephaly, however, the changes are more fundamental; in them there is microcephaly of a high grade. There is greater obliquity of the posterior limb of the Sylvian fissure; the bends or genua are absent in the fissure of Rolando; the fronto-parietal operculum does not develop; the external parieto-occipital fissure is notch-like; and there is obliquity of the orbital surface of the frontal lobe. In many cases characters are also to be found which recall the condition of the brain mantle in the apes; these are the so-called simian characters. In the Sylvian region, for instance, part of the island of Reil is exposed, and the frontal and orbital opercula are wanting. The intra-parietal sulcus is much less complicated than normal, and the so-called "Affenspalte" is present; the fissure of Rolando, also, is shallow and has smooth walls. In these high-grade microcephalics, therefore, there is evidence of an earlier arrest in development, about the third or fourth month of intrauterine life, it is said.

In another group of cases, the pseudo-microcephalics of Giacomini, there are changes of quite another kind of characters. There may be marked asymmetry of the brain, due to complete or partial atrophy of one hemisphere; there may be evident signs of fœtal encephalitis and marked consequent changes in the appearance of the cerebral surface; there may be various degrees of dropsical distension of the ventricles or hydrocephalus (the only specimen of microcephaly which I have examined was an instance of hydro-microcephaly); and porencephaly may be present.

The histological appearances of microcephalic brains have, unfortunately, been little investigated. Giacomini, however, comes to the conclusion that they are little different from the normal in typical cases. The cortical substance is smaller in amount; there are fewer nerve cells, and their development is less complete, and they show fewer processes. There is, therefore, according to Giacomini, a morphological rather than a histological character about the morbid anatomy of microcephaly; and this is supported by others, including P. Bull (*Norsk. Mag. f. Lægevidensk.*, 4 R., xvi. 1106, 1901).

It may be added that through the small size of the occipital lobes the cerebellum is not well covered by the cerebrum and is therefore more exposed to view. It is not enlarged; as a matter of fact it is commonly found to be diminished both relatively and absolutely. The various portions which go to make up the cerebellum, however, are present, and bear normal relations to each other; and their histological characters are not much altered.

(3) The *other parts of the nervous system* show deviations from the normal. As regards the spinal cord, there generally is micromyelia; the whole cord is diminished in size and the pyramidal strands of fibres (pyramidal tracts, columns of Goll, direct cerebellar tract) are the parts most affected, but the grey matter is also less in amount (A. Steinlechner-Gretschischnikoff, *Arch. f. Psychiat.*, xvii. 649, 1886). The state of the spinal cord is used, and with perfect fairness, by Giacomini as an argument against the local mechanical theories of origin of microcephaly which regard compression of the brain by the cranium, diminution in the size of the arteries supplying the cerebrum with blood, or internal hydrocephalus as causal factors. It is evident that micromyelia, without obvious changes in the microscopical appearances of the parts of the cord, points to an arrested growth and development of the whole cerebro-spinal system, and not to any effect localised in the cerebrum. The same remarks apply to the medulla oblongata, the pons, and the cerebral peduncles.

(4) *Associated malformations* occur in connection with microcephalus as with other teratological states; and I do not agree with Giacomini in thinking that their presence removes the case from the group of the true microcephalics. They are no longer *uncomplicated* microcephalics; that is evident; but it is not, I think, necessary to

cease to give them the name of microcephaly. The associated malformations affect, in the first place, the brain itself: they may consist in almost complete absence of the brain or in its very rudimentary development; in fusion more or less complete of the cerebral hemispheres (Rüdinger, *München. med. Wchnschr.*, xxxiii. 161, 185, 205, 1885; Aeby, *Arch. f. path. Anat.*, lxxvii. 554, 1879); in more or less complete absence of the corpus callosum (Onufrowicz, "Das balkenlose Microcephalengehirn Hofmann," *Diss. inaug.*, Berlin, 1887; Ducatte, *Thèse*, Paris, 1880; P. Broca, *Bull. Soc. d'anthrop. de Paris*, 2 s., xi. 85, 1876); and in anomalies of the hippocampus major, fascia dentata, etc. Outside the central nervous system there may likewise be malformations: of such are cyclopia (G. Raineri, *Osservatore*, xl. 767, 1889), hare-lip and cleft palate (C. Gunther, *Diss. inaug.*, Königsberg i. Pr., 1897), slight anomalies of the kidneys and uterus (D. Hansemann, *Zwei Fälle von Mikrocephalie mit Rachitis*, Stuttgart, 1899), etc.

The *teratogenesis* of microcephaly presents many unsolved problems. Of late years, however, some things seem to have become clear: it is not, for instance, now believed that the condition is due to cranial pressure, or to hydrocephalus, or to narrowness of the cerebral arteries, or to fœtal inflammatory disease (encephalitis). It is generally regarded as an arrested development. Karl Vogt (*Arch. f. Anthrop.*, ii. 129, 1867), writing in 1867, ascribed the arrested development to a partial atavism, and since then a great deal has been written and spoken on this subject. It cannot be denied that certain animal-characters are found in the microcephalic brain, but whether or not these are really simian reminiscences is very difficult of decision. Giacomini (*op. cit.*) thinks that there are some atavistic characters in microcephaly, but that these cannot be used as arguments for the theory of man's descent from the apes; the brain as a whole always retains the human imprint. The question at the present day has resolved itself into a discussion of the precise significance of simian or animal-characters in the human subject; in other words, it is recognised that it is a problem of germinal rather than of embryonic pathology. It may be held (as Mingazzini argues, *Biblioteca antropologico-Giuridica*, 1 s., xxii., 1895, cited by Cunningham, *loc. cit.*) that atavistic characters are latent and only appear when a disturbing element comes into the ontogeny of the part, but this does not fully explain their origin, it simply makes them dependent on the presence of the tendency to be malformed. It seems to me quite likely that when certain parts of the cerebro-spinal system do not develop, not only may the parts which remain pursue new ontogenetic paths, but other (and strange) structures may make their appearance; that they are atavistic in the narrow phylogenetic sense does not follow, for the plan of human ontogenesis may contain traces of other and simpler plans without being derived from any of them. The practical question is to find the cause which produces the arrest of development and so permits such aberrant structures to appear.

What has been discovered regarding the teratogenesis of microcephaly, although so limited in amount and in exactness, has seriously modified our views regarding its surgical treatment. If the brain be the *fons et origo* of the whole malformation, it can obviously be of little use to perform craniectomy in order to give more room for the cerebrum to expand. In practice this conclusion is supported by facts, for neither linear nor circular craniectomy, even when accompanied by division of the dura mater, have been followed by permanently good results. Surgery may yet devise means of benefiting this condition; but at present it is an antenatal problem, and there is urgent need to discover what it is that arrests cerebral development at the third month of intrauterine life and later.

Miscellaneous Malformations.

Cranial perforations of antenatal origin are occasionally met with. I saw a case in the Edinburgh Maternity Hospital in 1902 (Case No. 297). The child was born at the full time, its general development was good, and the weight was 5 lbs. 15 oz. The head diameters were fairly normal (O.M. = $5\frac{1}{4}$; O.F. = $4\frac{3}{4}$; S.O.B., $4\frac{1}{4}$ to $3\frac{3}{4}$). In the right parietal bone nearer the sagittal suture than the parietal eminence, but vertically above the latter, was a soft depressed area about the size of the pulp of the middle finger; posteriorly there was an edge of firm bone, but superiorly and anteriorly it faded gradually away into the surrounding bone. The area had a parchment-like feeling, and became tense when the child cried. A similar but smaller area was found in the same position on the left side, and there were two other spots lying posterior to it. The posterior fontanelle felt larger than usual. There was no history of syphilis in the mother, who was a I-para. Similar cases of symmetrical and congenital cranial perforations have been described by D. M. Greig (*Journ. Anat. and Physiol.*, xxvi. 187, 1892), Broca (*Bull. Soc. d'anthrop. de Paris,* 2 s., x. 192, 326, 1875), Larrey (*Bull. Acad. de méd.*, xxxi. 448, 1865–66), Sir W. Turner (*Edinb. Med. Journ.*, xi. 7, 133, 1865), and J. F. Goodhart (*Trans. Path. Soc. Lond.*, xxxvii. 364, 1886). They may indicate persistence of the parietal foramina. They do not always close after birth, for Greig's patient was twenty-five years of age.

Porencephaly is that state in which there is a funnel-shaped depression in the cerebral hemisphere leading down to and sometimes opening into one of the ventricles. Externally it usually communicates with the sub-arachnoid space. It may be associated with microcephalus, hydrocephalus, asymmetry of the cranium, and symmetrical flattening of the cranium. R. Sigmundt's inaugural dissertation (Strassburg i. E., 1893) gives many useful facts and statistics regarding this malformation, as does also R. Schattenberg's dissertation of Marburg, published at Jena in 1889. Apparently it may be either an antenatal condition or be acquired postnatally; in the latter case mental processes are not necessarily defective.

Absence of the corpus callosum (complete or partial) may occur without any apparent intellectual disturbances: M. S. Germano (*Cervelli* *di uomo mancante del corpo calloso,* Torino, 1874) has met with such a case, and others have been reported by Poterin-Dumotel (*Gaz. d. hôp.*, xxxvi. 47, 1863), T. O. Ward (*Lond. Med. Gaz.*, n.s., ii. 575, 1846), A. R. Urquhart (*Brain*, iii. 408, 1880–81), A. Bruce, with literature lists (*Rep. Lab. Roy. Coll. Phys. Edinb.*, i. 70, 1889), and L. A. Dunn (*Guy's Hosp. Rep.*, 3 s., xxxi. 117, 1889). Bruce thinks that most of the cases can be explained by arrested development at one time or another in antenatal life, and finds the chief cause in the primitive falx cerebri and septa lucida. *Absence, complete or partial, of the cerebellum* has also been observed, with or without other malformations (H. Salter, *Trans. Path. Soc. Lond.*, iv. 31, 1852–53; D. Fraser, *Glasgow Med. Journ.*, xiii. 199, 1880; R. Fusari, *Gazz. med. di Pavia,* i. 241, 1892; A. P. Gould, *Trans. Path. Soc. Lond.*, xxxiii. 6, 1881–82; Hitzig, *Arch. f. Psychiat.*, xv. 266, 1884).

The name *inter-parietal* or *epactal bone* is given to a small accessory bony nucleus found in the sagittal suture near its posterior end; other intercalary bones lying further forward in the same suture have been termed *pre-interparietals.* Wormian bones also occur in the lambdoidal suture. They have been regarded by some as due to arrested development, and by others as atavistic; and it has been stated that they are commoner in Peruvian skulls, hence the name *os Incæ* given sometimes to the inter-parietal. Several authors have written upon this subject (*e.g.*, R. Virchow, *Ztschr. f. Ethnol.*, xii. 1, 1880; G. Chiarugi, *Atti. d. r. Accad. di fisiocrit. di Siena,* 4 s., i. 31, 1889; G. Sergi, *Atti. Accad. med. di Roma,* 2 s., ii. 57, 1883–86; E. de Archangelis, *Ann. di neurol.*, xiv. 153, 1896).

A *third occipital condyle* may occasionally be found: it lies between the other two and in front of the foramen magnum, and may articulate with the odontoid process. Sometimes there is only an articular facette in this position. It is described by E. Ardù (*Giorn. d. r. Accad. di med. di Torino,* 3 s., xl. 408, 1892), who also gives several references (Sergi, Tafani).

A more or less perfect canal may be met with in the new-born infant (and even at later ages) leading from the sella turcica through the sphenoid bone to the pharynx; this is the *cranio-pharyngeal canal,* a remnant of the diverticulum of the pituitary body (Landzert). A median *canal in the basi-occiput* has also been noted, or, when it is imperfect, a slight depression on the basilar part of the bone, called the *foveola pharyngea* (Gruber). Rarely, an accessory bone, called the *basiotic,* is found between the occipital bone and the sphenoid; P. Albrecht (*Presse méd. belge,* xxxv. 121, 129, 137, 1883) described this bone as he found it in cases of anencephaly, cyclopia, anencephaly with cyclopia, and idiocy, as well as in otherwise normal crania; the bone has a bearing both upon the vertebrate theory of the skull and upon the occasional presence of a canal in the basi-occiput. Minor anomalies of the base of the skull (perforation of tegmen tympani, defect of lesser wing of sphenoid, etc.) have been described by J. Jænicke (*Diss. inaug.*, Kiel, 1877).

Various deformities of the cranium result from premature closure of one or several of the sutures. These are not always antenatal in origin, but some of them are, *e.g.* R. Förster's case of *dolichocephaly* from synostosis of the sagittal suture (*Jahrb. f. Kinderh.*, vii. 66, 1864). Other types of the dolichocephalic or long head are *sphenocephaly* (wedge-shape, due to compensatory enlargement in the region of the anterior fontanelle, the sagittal suture being ossified), *leptocephaly* (narrow-shape, due to synostosis of frontal and sphenoid), and *clinocephaly* (saddle-shape, due to synostosis of parietals with sphenoidal great wings or with the squamous temporals). The *scaphocephalic* or boat-shaped head is long and narrow, and the region of the sagittal suture is raised into a keel. There is marked shortness (*brachycephaly*) when the transverse sutures (*e.g.* naso-sphenoidal) are early closed: thus there is *pachycephaly* when there is synostosis between the parietals and the occipital, *oxycephaly* (sugar-loaf head) and *acrocephaly* (lofty-head) when there is compensatory growth at the anterior fontanelle, *platycephaly* (flat-head) when the temporals are united with the parietals, *trochocephaly* (round-head) when the frontals and parietals are partly fused near the middle of the coronal suture, and *plagiocephaly* (wry-head) when the frontal and parietal are united on one side. The small peaked head is called *scillocephaly*; *trigonocephaly* is a triangular head, and *tapeisocephaly* is a low head. The relation of these malformations to degeneracy is discussed by E. S. Talbot (*Degeneracy*, 1898).

Non-union of sutures may occur as well as premature union, and so lead to cranial malformations; but cases of this kind are rare at birth, for many of the sutures are normally open then. The frontal (metopic) suture, however, may be widely open (*metopism*), giving rise to a wide membranous space in this region (*vide* G. Vicarelli's case in an infant born by the Cæsarean section, *Arch. di ostet. e ginec.*, ii. 643, 1895, with literature). I have met with an instance in a specimen of phocomely; it is figured in the first section of this Manual, Fig 51, p. 351.

Omphalocephaly.

There is a most interesting monstrosity, whose exact place in any classificational system must remain doubtful, in which the head seems to protrude from the umbilical opening, and the heart (single or double) is seen on the nape of the neck or in the dorsal region. Dareste (*Production artificielle des monstruosités*, p. 359, 1891) is not using exaggerated language when he says, "Ce type est l'un des plus étranges que l'on puisse imaginer." It has not yet been met with in mammals, but is relatively frequent in chicks artificially hatched. Dareste noticed it in 1861, but did not then recognise its nature; in 1877 he gave an ingenious explanation of its teratogenesis (*Compt. rend. Acad. d. sc.*, lxxxiv. 1075, 1877), and he expanded his views later (*op. cit.*, p. 364, 1891). The anterior part of the intestine or pharynx is absent, being represented solely by the anterior part of the abdominal groove, so that there is not really an umbilical hernia of the head, for the umbilicus can hardly be said to exist. The anomaly appears to be due to strong inflection of the head (due to pressure, perhaps from the shell), which prevents the union of the prolongations forward of the lateral mesodermic folds; two hearts are produced in the same way. S. Warynski (*Thèse*, Genève, 1886) made some interesting experiments upon the artificial production of omphalocephaly and duplicity of the heart. E. Rabaud (*Compt. rend. Soc. de biol.*, 10 s., iv. 327, 1897; *Journ. de l'anat. et physiol.*, xxxiv. 247, 496, 545, 1898; *Thèse*, Paris, 1898) has also investigated the monstrosity, which he regards as due to the nervous system plunging towards the endoderm and enveloping itself in it. It is secondarily surrounded by the alimentary canal. The principal vessels and the notochord follow the nervous system. In a later paper, Rabaud (*Journ. de l'anat. et physiol.*, xxxvi. 619, 1900) has described two new conditions allied to omphalocephaly, and proposes to make a new group for them all, calling them *enenterians*, *i.e.* cases in which some part of the embryo is abnormally lodged in the alimentary canal, either anteriorly or posteriorly. When the lodgment is anterior, it is omphalocephaly; to posterior displacement Rabaud gives the name *ourentery*; when the notochord is elongated in the direction of the alimentary canal and in part clothed by it, the resulting monstrosity is called *eordentery.* They all are most curious teratological developments, and they may perhaps be found to have their homologues in some of the human amorphous placental parasites or allantoido-angiopagous twins.

CHAPTER XXI

Merosomatous Terata (*cont.*): Malformations of the Face and Mouth; Genal Fissures; Definition, Synonyms, Clinical Details, Morbid Anatomy, Varieties (Fronto-maxillary, Intermaxillary, Anomalous), Teratogenesis, Comparative Teratology: Median Fissure of the Face, of Upper Lip, of Nose, of Lower Lip: Hare-lip; Definition, Synonyms, Clinical History, Morbid Anatomy, Varieties (Unilateral, Bilateral, Simple, Complicated, Fissure of Jaw, Cleft Palate), other Associated Malformations, Comparative Teratology, Teratogenesis, Treatment: Fistula of Lower Lip: Fissure of the Tongue: Miscellaneous Malformations of the Face (Asymmetry, Brachyrhynchus, Cranium Progenium, Prognathism) and Mouth (Synchelia, Synechiæ, Tongue-Tie, Microstomia, Microglossia, Distomus, Macrostomia, Achelia, Brachychelia, Microchelia, Macrochelia, Dicheilus, Macroglossia, Congenital Teeth).

Having now passed in review the malformations of the Spine (Rachiterata) and of the Cranium (Cephalo-terata), we may proceed to the description of those of the Face (Prosopo-terata). This is a large and somewhat miscellaneous group of monstrosities and anomalies, for it includes not only those of the face proper but also those of the organs of special sense, the mouth, nose, eyes, and ears. If the reader will also keep in mind the complexity of the ontogenetic arrangements and rearrangements by which the framework of the face is constructed, how processes of the most various forms approach towards or recede from each other, coalescing, disappearing, and transforming in kaleidoscopic fashion, he will have little difficulty is realising the almost infinite variety of teratological formations which are to be met with in this region of the body. At the same time there is in the midst of this complexity an unexpected simplicity in the mode of origin of many of the prosopo-terata, for several of them can be evidently ascribed to the want of union between contiguous parts, to the persistence of embryonic clefts, or to the delayed arrival of certain processes and projections.

I have had some difficulty in selecting from so many malformations the most representative major types for special description. Thus with regard to the face proper and the mouth, hare-lip suggests itself as the standard type; but it is so fully explained and its characters are so fully made known in so many surgical and medical works that I have chosen rather to describe in some detail several malformations, including fissures of the cheek, of the face and nose, as well as of the lip and palate.

Genal Fissures.

A genal cleft or fissure of the cheek may be defined as a malformation of the lateral part of the face consisting in a cleft affecting the soft parts, or more rarely invading also the bones, arising during the embryonic period of antenatal life, and caused by delayed or irregular closure of the fissures between the fronto-nasal and superior maxillary and the mandibular processes.

It has also been termed "lateral fissure of the face," and this phrase has been given a classic form by Taruffi (*op. cit.*, vi. 338, 1891) in the somewhat unwieldy word *pleuro-prosoposchisis.* It is a much less common malformation than hare-lip; but Taruffi (*loc. cit.*, p. 339) has gathered together from medical literature nearly ninety cases, while in my 325 specimens there were three instances of lateral genal fissures (Nos. 23, 299, and 300, *vide* Figs. 25, 26, and 30).

Being a localised malformation, it has no characteristic antenatal clinical history, and any peculiarities in the pregnancy of the mother are with greater probability ascribed to the associated malformations, such as amniotic adhesions and hydramnios, than to the facial fissure. It is noteworthy, however, that it resembles hare-lip and differs from many other monstrosities in being much commoner in male than in female fœtuses: two out of my three cases were males, and in Taruffi's list of sixty-seven instances (in which the sex was stated) there were forty-one males and twenty-six females. The malformation does not necessarily prevent postnatal life unless it be complicated with some more serious anomaly (*e.g.* anencephaly), and it can very often be surgically dealt with, and improved, even if it be not quite cured. Before operation it is one of the most disfiguring anomalies in the whole range of Teratology, and fully justifies such epithets as "horrible" and "disgusting." In the long list of recorded cases which have been published, the following may be named as of special interest: J. Muraltus (*Acad. nat. curios. Ephem.*, cent. iii.–iv., 304, 1715); C. Nicati (*De labii leporini congeniti natura et origine*, 1822); V. Laroche (*Thèse*, Paris, 1823); E. Remacly (*Diss. inaug.*, Bonn, 1864); M. Pelvet (*Compt. rend. Soc. de biol.*, 3 s., v. 181, 1864); H. C. L. Barkow (*Beiträge zur pathologischen Entwickelungsgeschichte*, iv. Abth., 8, Breslau, 1871); J. Ruppersberg (*Diss. inaug.*, Marburg, 1872); C. F. Fritzsche (*Beiträge zur Statistik . . . der angebornen Missbildungen des Gesichts*, Zürich, 1878); J. H. Morgan (*Proc. Roy. Med.-Chir. Soc. Lond.*, ix. 94, 1882); R. Morian (*Arch. f. klin. Chir.*, xxxv. 245, 1887); J. Dreier (*Arch. f. klin. Chir.*, xxxviii. 269, 1888–89); O. Nückel (*Diss. inaug.*, Marburg, 1891); W. Bittner (*Prag. med. Wchnschr.*, xx. 440, 1895).

The *morbid anatomy* of these fissures of the cheek in many details is explicable by a glance at the embryology of the face, but in some points it shows puzzling divergences. We can, therefore, arrange all the cases in three chief groups: in one the fissure follows the line of the space between the naso-frontal process and that of the superior maxilla (*vide* pp. 34, 41); in a second it corresponds to the space between the superior and inferior maxillary processes; while in a third it has a direction which resembles none of the known embryonic facial clefts. Let us look briefly at each of these varieties.

(*a*) The *fronto-maxillary* or ascending fissure of the face has a general direction from the upper lip upwards towards the eye; it has also been called the "oblique" fissure of the face and "prosopo-ano-schisis" (Taruffi). In most instances it begins in the upper lip in a somewhat wide gap with red margins and floor, and passes upwards just outside the nose (in the naso-genal fold), to end in or near the lower eyelid of the same side. It may be unilateral or bilateral, and, except near its origin and termination, its walls are generally close together; it may even be cicatrix-like (antenatal cure?). In other instances it begins inferiorly in the ordinary position of hare-lip (inter-incisor) and extends up into the nasal cavity of one side, and so on to the inner angle of the eye, leaving in this case part of the ala of the nose external to it. This form, also, may be unilateral or bilateral; and both forms, when unilateral, would seem to show a preference for the left side. When bilateral, the fissures may be symmetrical; but more commonly they differ from each other. One may be short and wide and be limited to the tissues of the upper lip, while the other is narrow and is prolonged up to the eye and may even be continuous with a fissure in the lower eyelid; all intermediate degrees of extension may be met with. Again, there may be an ascending facial fissure on one side, and, on the other, a cleft running outwards from the angle of the mouth. In a few cases the fissure is prolonged beyond the eye into the temporal region, and sometimes there is a cleft of the upper eyelid as well as of the lower.

In most of the reported cases, the cleft affects the bones of the face as well as the soft parts; and it may pursue two courses in agreement with the varieties of direction shown by the cutaneous defect. It may, for instance, affect the alveolar margin of the upper jaw in the position corresponding to the union of the external part of the intermaxilla and the superior maxilla; then all the incisor teeth-germs are internal to the fissure, and the canine tooth-germ is external. Occasionally, what has been called a pre-canine incisor lies external to the cleft, an occurrence which cannot be satisfactorily explained by embryological processes. In other cases the cleft begins, as in ordinary hare-lip, in a space between the internal and external parts of the intermaxilla (between the inner and outer incisor tooth); now the inner part of the intermaxilla, the vomer, the nasal bone, the lachrymal, the ethmoid, and the inferior turbinate are all internal to the fissure, while the outer part of the intermaxilla, the superior maxilla, and the palatal process lie external. All possible grades of osseous defect may be met with, from a small crack in the alveolar margin of the jaw to a wide gap in the bone, passing through into the mouth and being continuous with a cleft in the palate. In the grave forms some parts may be actually absent, such as the intermaxilla or a portion of it.

In association with this variety of facial fissure we may meet with such anomalies as absence of one or both eyeballs, or cryptophthalmus, coloboma of eyelid, or amniotic attachments to the eye; there may also be encephaloceles of various kinds, anencephaly, hydrocephalus, and the like.

(*b*) The *intermaxillary* or commissural fissure of the face starts at the angle of the mouth and pursues an outward and upward course, which brings it to the temporal region or near the lobule of the ear. Various names have been given to it, such as hiatus buccalis, genal coloboma or hare-lip, commissural hare-lip, and macrostoma. Taruffi's term ("gonio-cheiloschisis"), although etymologically correct, is unfamiliar. The fissure may be bilateral or unilateral; and it is more often left-sided, when it is unilateral. It increases, in a disfiguring manner, the width of the mouth, and extends towards the lower end of the ear in a curve having its convexity external. When the fissure is bilateral the mouth may be equally and symmetrically increased; but more often there is asymmetry, and the cleft may reach further back on the one side than on the other (F. Rynd, *Dublin Quart. Journ. Med. Sc.*, xxxii. 45, 1861). The margins of the fissure are usually red, and, during life, the saliva flows out freely, excoriating the skin; Stenon's duct may be seen; if the individual survive birth the eruption of the teeth increases the deformity, and lactation, mastication, and articulation are rendered difficult. The bones of the face are not necessarily affected, but, if the fissure be directed more upwards towards the temple, the zygoma may be divided.

Associated malformations are fairly frequent. The commissural fissure may, for instance, be complicated by a fronto-maxillary one either on the opposite or on the same side of the face. Deformities of the external ear have been met with, as well as preauricular appendages. Less common is cleft palate; microcephaly, anencephaly, and exencephaly occasionally occur; as do also amniotic adhesions. In Pelvet's patient (*loc. cit.*) the upper jaw showed hypertrophy of its alveolar border, while the mandible was twisted and had a malformed condyle on the affected side.

(*c*) *Anomalous* fissures of the cheek are those which do not reproduce, in their direction and relations, any of the embryonic facial clefts. For instance, a fissure may begin at the angle of the mouth and pass upwards towards the outer angle of the eye, ending in the lower eyelid there; it may be associated with a defect in the bone stretching up between the germs of the canine and first molar teeth towards the infra-orbital foramen. Again, the fissure may begin midway between the outer angle of the mouth and the philtrum of the upper lip, and pass to a point in the lower eyelid between the outer and inner angles of the eye. No satisfactory explanation of these anomalous fissures is forthcoming, unless we accept the notion that the attachment of the amnion may cause a fissure at any spot whether there exists a natural embryonic fissure there or not.

It is unnecessary to enter in detail into the teratogenesis of fissures of the cheek. They are evidently arrested developments, and it is clear that, in some cases at least (as, for instance, in my three specimens), the arrest is due to amniotic pressure or adhesion. The embryonic clefts of the face do not close, and the fissures result.

It is true that the anomalous fissures do not thus meet with an adequate explanation; but it must never be forgotten that the arrest of one part allows other and contiguous parts to develop in new and unlooked-for directions, and thus irregularities may be introduced which, if we knew all the facts, would in the end support rather than weaken the theory. It is noteworthy that neither the fronto-maxillary nor the intermaxillary fissure is a common malformation in mammals other than man; when, however, they do occur they are apt to be more extensive, and have been known to open into the Eustachian tube and tympanic cavity, and to be associated with absence of the parotid gland and curious displacements of the upper and lower jaws (*e.g.* in schistocephalus retroflexus, Gurlt, *op. cit.*, 1877, p. 21). Perhaps the greater frequency of genal fissures in the human subject may be due to a peculiarity in the mode of development of the amnion in his case.

Median Fissure of the Face.

Early writers described the ordinary form of hare-lip as if it were median in position; then it was pointed out that it occurred laterally, at one or other side of the philtrum of the upper lip, and it was thought that true median fissures never were met with; finally, we now know that, although rare, clefts in the middle line, affecting the upper lip, the nose, and the lower lip, have from time to time been reported. These three are grouped together by Taruffi (*op. cit.*, vi. 288, 1891) under the one heading "meso-prosoposchisis."

(*a*) *Median fissure of the upper Lip* (Taruffi's name, "meso-epicheiloschisis," is altogether too cumbrous) is, in one sense, more truly a *hare-lip* than is the ordinary form of that defect, for the natural labial cleft in animals (hare, rabbit, sheep, some dogs) is mesial and not lateral in position. It is rare, however, in the human subject, and is not to be confused with the median loss of lip-tissue ("achelia") which is found in a case of ordinary bilateral hare-lip with absence of the structures of the intermediate philtrum. It consists rather in a triangular notch in the philtrum, or in a shortness of that part of the lip, so that it has a curved border. Sometimes there is a vertical groove or furrow in the philtrum, and, coexisting with it, a sulcus in the intermaxillary bone and palate. Sometimes there is an actual fissure dividing the whole substance of the lip in the position of the philtrum; the fissure then has the same characters as the fronto-maxillary one was found to have; the intermaxilla may, at the same time, be grooved, fissured, or incomplete. Cases are recorded in which both the philtrum and the intermaxilla were entirely wanting, but these approximate so closely to the monstrosity termed "cebocephalus" that I shall consider them under that heading (*vide* p. 405). Flattening of the nose may be noted; but grave defects of that organ, of the brain, and of the deep parts of the face (the ethmoid, palate) are generally found only in the advanced degrees of median fissure which almost come under the designation of "cebocephalus." Associated malformations of a less severe type are preauricular appendages, hypertrophy of the lower lip (*macrochelia*), polydactyly, and shortness of the limbs. A congenital *fistula* of the frænum of the upper lip has been noted (Lannelongue et Ménard, *Affections congénitales*, i. 264, 1891); it perhaps indicated a partly cured fissure. Median fissure of the upper lip would appear to be less common (as a malformation) in animals than in man.

(*b*) *Median fissure of the Nose* ("meso-rhinoschisis," Taruffi) is rarer than median fissure of the upper lip, but is rather less rare in some of the mammals than in man. There is a groove or sulcus, or simply a cicatrix (antenatal cure?), in the middle line of the dorsum of the nose, which may affect the whole organ or only a part of it, and may be shallow or deep; it may be restricted to the nose (J. Poland, *Pediatrics*, i. 401, 1896), or extend on to the forehead, or be continuous inferiorly with a hare-lip. Two illustrative instances, with some references to the literature of the subject, are given by D. Nasse (*Arch. f. klin. Chir.*, xlix. 767, 1895); and some years ago Dr. Paul Liebrecht of Liège sent me a reprint of his article on a case of bifid nose with *median* (not lateral) fissure of the upper lip (*Difformité congénitale du nez*, Bruxelles, 1876). Sometimes the fissure is so deep that the nose is divided into two parts, which may lie side by side and be in every way symmetrical, or may be separated from each other and unlike in appearance. Taruffi's case (*op. cit.*, vi. 514, 1891) was particularly interesting: the nose consisted of two longitudinal halves, of which the left was fairly normal in appearance, but the right constituted a mobile tube or trunk (like the proboscis so often found in cyclopia, *q.v.*), with a circular depression in its free end and a small opening at the bottom of it; there were two palpebral colobomata in connection with the right eye. A still deeper fissure of the nose may be met with in which the whole face is split (*schistocephalus bifidus*, Gurlt; *meso-cheilo-rhinoschisis*). On the other hand, the nasal groove may be both short and shallow, and at its upper end there may be seen a little fistulous opening (J. Hoppe, *Med. Ztg.*, n.F., ii. 164, 1859). The coexistence of a *median fistula* of the nose and a median fissure has suggested to Lannelongue and Ménard (*Affections congénitales*, i. 372, 1891) the question whether when the fistula occurs alone it represents a fissure which has nearly quite closed. It may be noted that in cases of dermoid cysts of the nose it is not uncommon to find a fistula leading down to the little tumour; it is easy to imagine a fissure which closes, including, as it does so, some dermal elements and so produces the dermoid, while the communication with the surface is kept open by the secretion.

With regard to the production of the fissure itself, various opinions have been expressed. The wide separation of the two halves of the nose has been ascribed to the action of an amniotic band or adhesion, and such a case as that figured by Lannelongue and Ménard (*op. cit.*, p. 371, fig. 33) proves this to the degree of demonstration. On the other hand, some observations would seem to show that a mesial meningocele (O. Witzel, *Arch. f. klin. Chir.*, xxvii. 893, 1882–83), or a tumour of one kind or another, may prevent the natural union of the two halves of the nose. The more shallow grooves have been regarded as arrested developments produced perhaps by amniotic pressure, perhaps by excessive thickness of the nasal septum.

This malformation is not to be confused with duplicity of the nose, an instance of which, reported by Regnault (*Bull. Soc. d'anthrop. de Paris,* 5 s., ii. 333, 1901), was referred to in Chapter XII. (p. 233). In these cases, parts of two faces are present, while in the subject now under discussion there is less than one face. At the same time it may be very difficult from a superficial examination to classify correctly all cases.

Median fissure of the nose occurs among the lower animals, as a "normal deformity," so to say, in some dogs (*e.g.* pointers and setters), and as a true teratological state in other mammals. Gurlt (*Ueber thierische Missgeburten,* 18, 1877) has subdivided the cases into two groups, *schistocephalus bifidus* and *s. semibifidus*; the second of these contains the rarer specimens, but they more closely resemble what is found in the human subject.

(*c*) *Median fissure of the lower Lip* ("meso-hypocheiloschisis," Taruffi), little known before the nineteenth century, is even now a rare occurrence. Sufficient observations have been made, however, to show that it may exist in all grades from a slight notch in the lower lip in the median line to a large and complete fissure extending down through the lower jaw in the position of the symphysis. It has been known to occur in a family in which there were several instances of ordinary hare-lip (E. Hamilton, *Dublin Journ. Med. Sc.*, lxxii. 1, 1881); and its presence may lead to constant loss of saliva and resulting bad health. Bouisson (*Dict. encycl. d. sc. med.*, viii. 640, 1868) has noted a case in which a slight antero-posterior groove in the lower lip was the only anomaly; Parise (*Bull. gén. de thérap.*, lxiii. 269, 1862), on the other hand, has seen a median labial fissure associated with division of the lower jaw and a bifid state of the tongue, and continued as a cicatrix to the level of the sternum. In one of Hamilton's cases (*loc. cit.*) there was a cleft palate and an ordinary double hare-lip in addition to the median fissure of the lower lip; at each side of the fissure was a small nodule in the lower lip, and when the mouth was shut these filled up the deficiencies in the upper lip. Other associated malformations have been club-foot, and tumours (osteomata, teratomata) in the middle line of the lower jaw; and to the latter some importance has been ascribed as teratogenic agencies in the production of the fissure. The anomaly has been met with in the lower animals, both in mammals and birds, and has generally been complicated with division of the tongue.

All these three varieties of median fissure (of upper and lower lips and of nose) have been successfully treated by the surgeon; but the cases associated with deep-seated osseous defects of the jaws are not hopeful.

Labium Leporinum (Hare-Lip).

Ordinary hare-lip (labium leporinum, lateral nasal fissure, lateral labial fissure, cheiloschisis, pleuro-epicheiloschisis) is so fully described in works upon Surgery that I do not enter into many details here, but from the standpoint of Teratology it is necessary to refer to certain matters in connection with it.

It is a malformation which has been known from very early times, it has a large literature, and has long engaged the attention of the surgeon and exercised his skill in devising reparative and plastic operations. It is also a frequent malformation, and is apt to occur in several members of the same family (family prevalence). Many instances of this phenomenon have been recorded: Mercer Adam (*Month. Journ. Med. Sc.*, Edinburgh, 3 s., ix. 402, 1854) met with the case of a woman whose five children all had hare-lip; and Meckel (*Handbuch der pathologischen Anatomie*, i. 19, 1812) refers to Anna's observation of a man who had by his first wife eleven children, nine of whom were born dead, and two alive, with hare-lip, and by his second wife four children, two of whom had the same deformity and one had cleft palate. Direct heredity, however, may also be noted, as in R. G. H. Butcher's case (*Dublin Journ. Med. Sc.*, lxiii. 426, 1877) in which both mother and child had double complicated hare-lip, with entire absence of the palate. C. J. Trew, also, met with a man whose palate showed a cicatrix; by his wife, who was normally formed, he had seven children, three females had hare-lip and cleft palate, while two boys and two other girls were normal (*Nova Acta phys.-med. Acad. nat. curios.*, i. 445, 1757). Hare-lip seems to have a preference for the male sex, for if the statistics of T. Bryant (*Guy's Hosp. Rep.*, 3 s., vii. 3, 1861), C. F. Fritzsche (Zürich, 1878), and E. Herrmann (*Diss. inaug.*, Breslau, 1884) be put together we find 180 males and 118 females, or 60·405 per cent. and 39·595 per cent. respectively.

Morbid Anatomy.—Hare-lip may be simple or complicated, unilateral or bilateral. Simple hare-lip, when *unilateral*, is generally on the left side. The fissure passes from the free edge of the upper lip just outside the philtrum towards the nostril of the same side. It varies within wide limits as to its extent: it may reach quite to the opening of the nares and constitute a gaping triangular space with the apex upwards; it may stretch as a narrow fissure involving half the thickness of the lip and reaching half-way to the nose; or it may be a mere notch in the edge of the lip. Indeed, in some cases it may be only a shallow sulcus or cicatrix, and in these instances it is supposed that there has been antenatal cure of the deformity; cases of this kind were reported by Chauvin (*Rev. méd. franç. et étrang.*, ii. 226, 1838), Cuthbert (*Trans. Edinb. Obst. Soc.*, i. 51, 1870), M. Bartels (*Arch. f. Anat., Physiol. u. wissensch. Med.*, 595, 1872), P. Seiler (*Diss. inaug.*, Berlin, 1882), Lannelongue and Ménard (*Affections congénitales*, i. 273, 1891), and several others. It is not, however, quite clear that this is the real explanation of the anomaly, for no cicatricial tissue has been found; it may be simply a less complete defect of the lip (involving, for example, only the muscular tissue), and the occurrence of a case of fissure on one side and cicatrix-like groove on the other may be regarded as supporting this idea (Fritzsche, *op. cit.*). The fissure extends obliquely across the lip to the nostril, partly on account of muscular action which draws the outer edge outwards; the edges are covered with mucous membrane, which may show streaks and slight furrows (cicatrices?), and the inner edge is shorter and thicker than the outer; and it (the fissure) usually corresponds topographically to the space in the upper jaw between the internal and external incisor tooth. No case seems to have been put on record of a fissure affecting only the upper part of the upper lip and leaving the margin united, and from this occurrence it has been concluded that the natural fissures of the face close from above downwards. The philtrum may lose its natural concavity even in the unilateral variety of hare-lip; it does so very completely in the bilateral form, for it is then usually convex. One nostril may be flattened, and the nasal septum may show a convexity affecting the opposite side from that on which the fissure exists.

The *bilateral* form of simple hare-lip is rare, for when there is a double fissure the alveolar border of the maxilla is commonly affected. When it does occur, the fissures have appearances such as have been already described. Of course there is now an isolated median portion of the upper lip (median tubercle or lobule), which is somewhat stunted and leaves the incisor teeth exposed (in postnatal life), and is attached either to the gum or to the nasal septum. In some cases the median tubercle may be so reduced in size as to give to the upper lip the appearance of a median fissure. Its histological characters have been investigated, and it has been found to consist of skin (with hairs and sebaceous and sudoriparous glands), connective tissue with numerous tortuous capillaries, the naso-labial muscle, and a mucous membrane in which there are no glands (Lannelongue and Ménard, *op. cit.*, p. 271). To bilateral hare-lip Taruffi gives the name dipleuroepicheiloschisis.

Hare-lip *complicated* with fissure of the alveolar arch of the upper jaw (*cheilo-gnathoschisis*) may be unilateral or bilateral. It was formerly maintained that the fissure in the bone corresponded to the suture between the premaxilla and the superior maxilla, and that therefore the incisor teeth (after eruption had taken place) lay internal to it; but it is now known that most often the cleft runs through the premaxilla and separates the central from the lateral incisor tooth. The fissure, therefore, corresponds to the interincisor suture; which probably indicates that each premaxilla is developed from two ossific nuclei lying side by side. The fact that this is the commonest position for the cleft was established by P. Albrecht (*Centrlbl. f. Chir.*, xi. 521, 1884; *Deutsche Ztschr. f. Chir.*, xxi. 201, 1884; etc.), and although some cases have been reported which cannot be satisfactorily explained by the theory associated with it, yet it must be admitted to be a correct observation. For the fissure to run between the premaxilla and the superior maxilla, outside the region of the incisor teeth, is quite exceptional. Sometimes a supernumerary incisor tooth is met with (a precanine incisor), due probably to cleavage of the dental germ of the lateral incisor; this may explain some of the anomalous cases. As a rule, however, the two central incisor germs are in the central bone between the two fissures (when the hare-lip is bilateral), and one lateral incisor germ is outside the fissure on each side. Through the presence of the bilateral fissures (which usually stretch back to the foramen incisivum) the premaxillary bones are displaced forwards and form part of the median tubercle. Cleft palate usually but not constantly accompanies fissure of the alveolar arch. Exceptionally the mucous membrane may be continuous while the underlying alveolus is split.

Cleft palate (palatoschisis) constitutes one of the malformations which, when associated with labial fissure, constitutes complicated hare-lip. It is true that cleft palate may occur alone, but, when it does so, it shows the same characters as when combined with hare-lip. It exists in various grades. It may, for instance, consist in a bifid state of the uvula, in a fissure of the soft palate alone, or in different degrees of cleavage of the osseous palate and of the mucous membrane which covers it. In its most marked form and when combined with double hare-lip and fissure of the alveolar arch it constitutes one of the most disfiguring of all the teratological states; there is then a mesial gap in the roof of the mouth, producing a bucco-nasal cloaca, hanging down into which is the more or less altered vomer, and projecting into the sides of which are the inferior turbinated bones. It may also be unilateral, and then the fissure runs along by the side of the middle line, and the vomer is attached to the unaffected side of the palate. Sometimes, while there is a bilateral fissure, there is asymmetry, the deformity being more extensive on the one side than on the other. In a few rare cases the osseous fissure has been covered with intact mucous membrane, or with cicatricial tissue; and in one or two instances simply a slight depression or groove may be found in the palate, which has been interpretated as indicating antenatal cure (H. Chrétien, *Thèse*, Paris, 1873). It has to be borne in mind that in well-marked cases the defect is not restricted to the actual palate (hard and soft), but may extend to the nasal septum and neighbouring parts, which may be longer or shorter or of less or greater dimensions vertically; thus it happens that surgical reparative operations may be partial failures, for something more is needed than merely bringing separated parts into contact. On the other hand, the cure of a hare-lip may be followed by an improvement in the state of the cleft palate, showing that Nature tends to make good deficiencies under improved conditions. It is unnecessary, in this work, to do more than remind the reader that grave disabilities attend the child born with a cleft palate and hare-lip; lactation and, later, articulation are seriously interfered with.

Associated Malformations.—Hare-lip and cleft palate may be found associated with almost every other type of monstrosity. They may, for instance, complicate anencephaly and cyclopia, and in one of my cases of anencephaly (Specimen No. 155) there was bilateral labial and palatal fissure; club-foot, cranial asymmetry, and hernias of various kinds are common concomitants; the rarer deformities known as cebocephalus and trigonocephalus may also be associated; and I have met with a case in which there was double hare-lip in

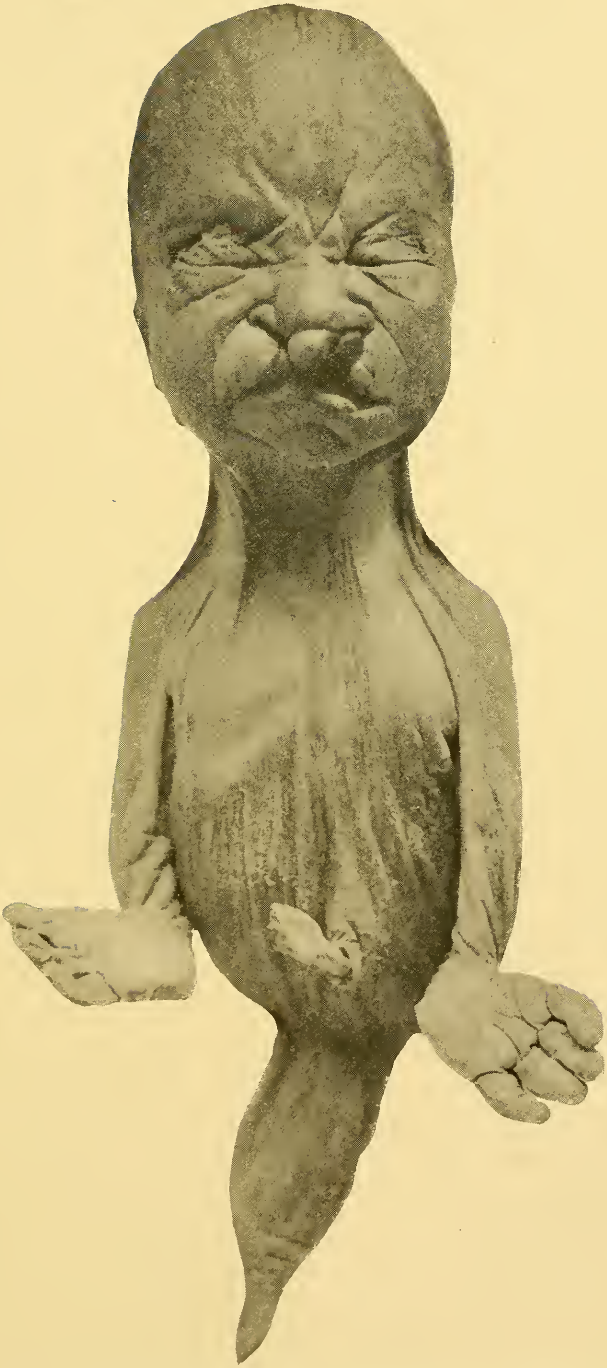


Fig. 63.—Uromelic Sympodial Fœtus with Double Hare-Lip. Specimen No. 250.

a uromelic sympodial fœtus (Fig. 63, Specimen No. 250). Again, hare-lip may be complicated by the presence of genal fissures, by preauricular appendages, by deformities of the ears, and by anomalies of the eyes. I have also seen a case of double fistula of the lower lip (Case No. 221) and another of fœtal ascites (Specimen No. 229).

Comparative Teratology.—Hare-lip is somewhat rare in the mammalia (other than man); it is rarer in them than cleft palate. Further, median and lateral fissures have not always been distinguished. Gurlt (*Lehrbuch der path. Anat. der Haus-Saugethiere,* ii. 130, 1832) gave to mammalian hare-lip the name *schistocephalus fissilabrus,* and to cleft palate that of *schistocephalus fissipalatinus.* Cleft palate may not infrequently occur alone without labial fissure, and it would appear to extend forward in the middle line between the premaxillæ and not between them and the superior maxillæ or between the two parts of each premaxilla as in man. As I have so often pointed out, these peculiarities of Comparative Teratology must have a meaning and may yet throw light both upon Human Teratology and Human Embryology. It may be noted as an interesting etiological suggestion that, in the case of lionesses in the London Zoological Gardens, the absence of bones from the food seemed to be associated with the birth of young lions with cleft palates.

Teratogenesis.—The notion of maternal impressions and of the action of the tongue of the fœtus and of its nails as factors in the production of hare-lip and cleft palate need not be considered. Further, the presence of a tumour (teratomatous or other) in the fissure and possibly producing it, is so exceptional an occurrence that it cannot be utilised for the explanation of cleft palate in general. Nearly every one is prepared to admit that these fissures are the result of arrested development, even if all are by no means at one as to the precise mechanism by which the arrest is initiated. There is strikingly little evidence that in this particular instance amniotic bands are effective in teratogenesis; they are notably so in the genal fissures (fronto-maxillary, etc.), but are not seen in hare-lip. It is still open to us to suppose that amniotic pressure may be the arresting cause; but it must be admitted that very little light is forthcoming on this point. Further, although it must be admitted that the fissure is the result of arrested development, many difficulties connected with the ontogenesis of the face present themselves; indeed, the whole question of the nature, origin, and relations of the premaxillæ or intermaxillary bones is bound up with this teratological problem. Until about twenty years ago it was generally believed that the fissures in hare-lip indicated a persistence of the original divisions between the maxillary processes and the side of the fronto-nasal process; and there was a most satisfactory simplicity about the explanation which was thus apparently established. Apparently simple explanations of matters embryological and teratological have, however, on more occasions than one turned out to be fallacious, and it was so with hare-lip. It was pointed out by P. Albrecht that the fissure in the upper jaw (in hare-lip) did not mark off the intermaxilla (or premaxilla) from the superior maxilla as had been supposed, but passed right through each premaxilla dividing it into two parts, the inner of which was united with its fellow of the opposite side to form the osseous part of the median tubercle, while the outer was conjoined with the superior maxilla. The central incisor tooth was commonly carried by the inner half of the premaxilla and the outer incisor by the outer half, so that when the bilateral fissure was present there were two incisors attached to the median tubercle and one to each side of the jaw outside the fissures. The fissure then marked the division between the outer and inner part of the premaxilla, and it was to be considered that there were in the human subject not two but four premaxillæ. The cleft in the bone indicated not the embryonic fissure between the fronto-nasal process and the superior maxillary process, but the space between the internal and external nasal processes of the fronto-nasal process; it was a cleft entirely within the fronto-nasal process. The median tubercle in hare-lip, therefore, represented not the whole of the two premaxillæ but only their inner parts. It cannot, however, be stated that this question is settled. Many difficulties stand in the way, most of which are connected with the number and arrangement of the incisor teeth, which are cut in connection with hare-lip. I think too much has been made of the morphological significance of these teeth both in the arguments for and in those against Albrecht's views. After all, it is not to my mind an unthinkable theory that the cause, which arrests the development of the face and makes permanent what ought to be a transitory arrangement of parts, may also act upon the dental germs in the jaw and lead one germ to atrophy and another to increase in size and perhaps divide into two. The facts of embryology must first be thoroughly investigated (teratological developments being utilised as hints to direct research), and then the general principles of teratogenesis must be applied to the scrutiny of the results; if this be done, I feel sure that the actual mode of production of hare-lip and all other malformations will be made plain. Of course this does not mean that the cause which leads to the arrested developments will be discovered, although we may be in an infinitely better position to make surmises regarding its nature; we shall then, I expect, find we are dealing with the germinal factor.

Treatment.—As I have pointed out several times already, this work is not a Manual of Surgery but of Antenatal Pathology and Hygiene, and therefore it does not fall within its sphere to discuss the various operative procedures to correct deformity. I may, however, point out to the surgeons that Nature encourages them by her own successful antenatal reparative essays, and that they will find it well worth their while to study all that is known bearing upon the mechanism of the production of the deformity. Especially ought the associated anomalies in such neighbouring parts as the vomer, the premaxilla, and the nasal chambers to be attentively investigated before operation, and provided for during operation if the final result is to be good. Since hare-lip and cleft palate have been repeatedly shown to be hereditary, it may quite reasonably be asked whether antenatal hygiene ought not to try to prevent their transmission; possibly lime salts given to the mother may be efficacious; possibly, also, they may not. But trial may be made.

Fistulæ of the Lower Lip.

I may here refer very briefly to a curious and almost inexplicable malformation of the lower lip which may be met with sometimes in connection with hare-lip, sometimes alone. I mean bilateral fistulæ of the lower lip. In February 1899, Mr. Cotterill kindly gave me an opportunity of examining a case of this kind: it was that of a young girl who had also hare-lip; but the most noteworthy defect was not in the upper but in the lower lip, where there were two fistulæ, symmetrically arranged one on each side of the middle line. The appearance they presented was exactly like that produced by firmly pressing the two central incisor teeth of the upper jaw against the lower lip. It was stated that the girl's grandfather had exactly the same malformation.

The first case of this peculiar malformation to be reported seems to have been that of J. N. Demarquay (*Gaz. méd. de Par.*, 2 s., xiii. 52, 1845); in it the fistulæ passed downwards under the mucous membrane of the lip towards the frænum. Since then a number of instances have been put on record, including those by Béraud (*Bull. Soc. de chir. de Par.*, 2 s., ii. 233, 1862), J. J. Murray (*Brit. and For. M.-Chir. Rev.*, xxvi. 502, 1860), Richet (*Bull. Soc. de chir. de Par.*, 2 s., ii. 230, 1862), Depaul (*ibid.*, p. 349), L. A. Ranvier (*Compt. rend. Soc. de biol.*, 3 s., iii. 93, 1862), Rose (*Verhandl. d. Gesellsch. f. Geburtsh. in Berlin*, xxi. 82, 1869), U. Trelat (*Journ. de méd. et chir. prat.*, xl. 442, 1869), Demarquay (*Bull. Soc. de chir. de Par.*, 2 s., ix. 111, 1869), Lannelongue (*Bull. et mem. Soc. de chir. de Par.*, n.s., v. 617, 1879), T. Sympson (*Brit. Med. Journ.*, ii. for 1882, 1145), H. H. Clutton (*Trans. Path. Soc. Lond.*, xxxviii. 446, 1887), Madelung (*Arch. f. klin. Chir.*, xxxvii. 270, 1888), O. Zeller ("Ueber angeborene Unterlippenfisteln," *Diss. inaug.*, Berlin, 1891), Lincoln de Castro (*Gazz. d. osp.*, No. 122, 1894), L. H. Miller (*Med. Rec.*, xlix. 87, 1896).

Family prevalence as well as direct heredity have been specially associated with this anomaly. In the case that I saw, the grandfather of the patient had the same defect. Demarquay's subject had four brothers and his mother similarly affected. Lincoln de Castro's record was a most remarkable one: there were three individuals, a brother and two sisters, who had each a double fistula in the lower lip; the father was normal but the mother had a cleft palate; a seven months' fœtus that lived fourteen days had the same condition of the lower lip; so had the maternal grandfather; and the maternal grandmother had given birth to a fœtus with hare-lip and incomplete closure of the thoracic and abdominal cavities. It was truly a teratological family! Murray reported four cases in the same family, while several other members had hare-lip alone.

The cases closely resembled each other; but in Lannelongue's patient the fistulæ opened into a single cavity, and in the instances recorded by Trelat and Clutton there was in addition a fold of mucous membrane dividing the lower lip into an anterior and a posterior portion. The part of the lip bearing the fistulæ may be hypertrophied and project almost like a proboscis.

As has been pointed out already, the anomaly is often associated with double hare-lip, and in its absence with cleft palate. Club-foot is also common.

Since some fluid resembling saliva exudes commonly from the fistulous tracts, surgical interference has been occasionally invoked to remove the inconvenience resulting from this, generally with success.

The teratogenesis of the condition is obscure. The idea of fœtal inflammation of one or more of the labial mucous glands is unsatisfactory. The most probable view is that here we have an indication of the presence of an intermaxillary bone in the lower jaw; the fistulæ, therefore, are arrested developments at a stage when ontogenesis was nearly completed, and the anomaly falls into line with the minor grades of hare-lip. Bland-Sutton (*Tumours*, p. 347, 1903) calls them "mandibular recesses," and ascribes them to faulty coalescence of the intermandibular fissure.

Fissure of the Tongue (*Schistoglossia*).

Cases of median fissure of the tongue are on record, but they are rare, and they almost always are overshadowed by the associated malformations. G. Barling (*Brit. Med. Journ.*, ii. for 1885, p. 1061), for instance, saw a case in which there was a V-shaped cleft in the anterior part of the tongue in association with cleft palate, and at the apex of the V was a median lobe which was removed by the surgeon to allow room for the tongue in the mouth. Another case in which there was both cleft palate and defective development of the lower jaw was reported by A. Brothers (*Med. Rec.*, xxxiii. 109, 1888); and yet another by G. O. Beaudry (*Union méd. du Canada*, iv. 342, 1875). In most of the other cases, *e.g.* Taruffi's anencephalic fœtus with two mouths (*op. cit.*, vi. 527, 1891) and Windle's observation on a calf (*Journ. Anat. and Physiol.*, xxii. 432, 1888), there are signs of a deep-seated duplicity affecting the whole head. The anomaly may be ascribed to excessive development of the two lateral structures which form the tongue, or to defective growth of the median part (tuberculum impar). When the three parts all develop but do not unite together a trifid tongue may result, as in Gurlt's calf (*Ueber thierische Missgeburten*, p. 20, pl. xii., fig. 56, 1877).

Miscellaneous Malformations of the Face.

I have considered with some degree of detail a number of facial and buccal deformities, characterised by absence of union of embryonic parts (*e.g.* fissures of cheek, mouth, palate, and fistulæ of lips); but there are still many other facial anomalies which I must briefly refer to.

Facial Asymmetry of various kinds may be met with. I have already referred to *unilateral hypertrophy* or atrophy of the face (p. 264), but it must be borne in mind that the unilateral enlargement may be due to several different causes, including true hyperplasia, neoplasms (such as angiomata), and even teratomata. When the last-named condition is present the asymmetry may be extreme. Hemiatrophy of the face, often associated with congenital torticollis (Lannelongue et Ménard, *Affections congénitales*, i. 498, 1891) may occur in the fœtal rather than in the embryonic period of antenatal life, and be due to uterine or amniotic pressure; there is usually cranial asymmetry in addition. The resulting facial obliquity has been termed *prosopus varus*. Facial asymmetry, however, may also arise in the embryonic period: of the forms due to marked defect of the lower jaw I shall speak in connection with otocephalus and synotia; but I may briefly notice here the results of imperfect development of the upper jaw. The name *brachyrhynchus* has been given to those cases in which the upper maxillæ are short, the nose and nasal cavities small, and the lower jaw projecting. It is more common and more characteristic in the lower animals than in man. It may be met with in birds, in fishes, and in mammals, and is indeed a racial feature of certain kinds of dogs. In the human subject it is most often associated with such extreme malformations as cyclopia and cebocephalus (*q.v.*), but may occur alone; and it is possible that in some grave cases (as in that by W. Ross, *Trans. Obst. Soc. Lond.*, ix. 31, 1868) the superior maxillary bones may be almost absent. In the deformity known as *cranium progenium* the appearances suggest increased size of the lower jaw rather than diminished size of the upper; but there are facts (L. Meyer, *Arch. f. Psychiat.*, i. 334, 1868) which make it probable that it is small size of the basis cranii along with defective growth of the upper jaw that, after all, is the determining factor.

Congenital Prognathism, although normal in some races of mankind (African negro, etc.), is a malformation in orthognathous peoples; the projection of the jaws and the small size of the forehead are its striking features. These various malformations are apt to be associated with cranial anomalies, with microcephaly, nanocephaly, and the like, and with mental defects when the individuals survive their infancy.

Miscellaneous Malformations of the Mouth.

Astomus, or complete absence of the mouth, will be considered with aprosopus (in which nose and eyes as well as mouth are wanting); but, at this point, reference may be made to *synchelia* or *syncheilus*, by which name is meant apparent absence of the mouth or fusion of the lips. Congenital closure of the mouth due to synchelia is an exceedingly rare malformation, and in this respect contrasts strongly with the comparative frequency of anal imperforation. A case was reported by A. E. Büchner (*Acta Acad. nat. curios.*, ii. 210, obs. xcvi., 1730) in 1730 and described as "infans ore clauso et concreto natus"; it was accompanied by a *scholion* dwelling on the question of how this astomatous fœtus had been nourished in utero. Some other cases have been observed, including one by Taruffi (*op. cit.*, vi. 531, 1891), but generally in association with other defects. When it occurs alone, surgical interference may prove quite successful in establishing an opening. Combined with it may be various *buccal synechiæ*, such as adhesions between the soft palate and pharyngeal walls, or between the velum palati and the arch of the palate, between the tongue and the floor of the mouth (*tongue-tie*) or the roof of the mouth (*ankyloglossia superior*) or the gums, or between the cheeks, lips, and gums. Union of the gums together is very rare (Carter, in Garretson's *System of Oral Surgery*, p. 433, 1873). These synechiæ may be malformations developed not in the embryonic but in the fœtal period of antenatal life.

Microstomia or microstomus is the condition in which the oral aperture is very narrow from side to side, and the lips very small. When the mouth is reduced to a small foramen or vertical fissure it may be expected that grave defects of the mandible coexist with it. It is rare for it to be met with apart from other malformations (W. Duncan, *Trans. Obst. Soc. Lond.*, xxxvii. 16, 1895); but a few cases have been reported in which the associated anomalies were comparatively slight (F. A. von Ammon, *Journ. d. Chir. u. Augenh.*, n.F., iii. 250, 1844). *Microglossia* may also be met with.

Distomus or "double mouth" is a very rare monstrosity in a fœtus otherwise single: it is, of course, commonly found in double terata. Even when the fœtus is not obviously double, the condition of distomus may, when fully investigated, show signs of duplicity in neighbouring parts. This was the case in Taruffi's very remarkable anencephalic fœtus with sympodia (*op. cit.*, vi. 528, 1891), in which there was a very wide mouth and two lower jaws lying side by side, the oral aperture was closed in the middle line. In O. Israel's specimen (*Diss. inaug.*, Berlin, 1877) the second oral opening was at the left side of the lower part of the face, where there was a supernumerary ramus of a lower jaw and a rudimentary tongue; the left ear was also malformed, but the child was otherwise normal. Such cases occur in the lower animals, as in the sheep (K. von Kostanecki, *Arch. f. path. Anat.*, cxxiii. 405, 1891).

Macrostomia or macrostomus is an unusual width of the mouth. It has been already described under the head of commissural fissures of the face, and is very rare apart from these defects. Taruffi (*op. cit.*, vi. 534, 1891) refers to a case by G. Friderici as an instance of non-fissural macrostomus; but an inspection of the original work (*Monstrum humanum rarissimum recens in lucem editum*, Lipsiæ, 1737) and a reference to the astonishing coloured plate which accompanies it (which are in my library) has convinced me that it is not an instance of large mouth but of open mouth ("os mire apertum"), without a trace of lips (*achelia*). A famous historical example of macrostomia was Margaret Maultasche, who married Prince John of Bohemia in 1342.

Brachychelia or brachycheilus is the name given to anomalous shortness of the lip, usually the upper. Of course this deformity is often met with in connection with hare-lip when atrophy of the philtrum is almost constant; but it also occurs as the sole deformity. J. Schenckius à Grafenberg (*Observationum Medicarum*, lib. i. p. 225, Francofurti, 1609), for instance, refers to the case of a woman (" honesta matrona ") born with a short upper lip (" labio curto nata ") which did not cover her teeth. *Microchelia* is a somewhat synonymous term. Anomalies of the frænum of the lip have been reported (shortening, triple character, etc.).

Macrochelia or macrocheilus, enlargement of the lips, is a more common deformity than brachychelia. Sometimes it is the upper lip alone which is affected (*epi-macrochelia*, Taruffi) and the tongue may join in the enlargement (*macroglossia*); only one-half of the lip may be large and there may then be unilateral hypertrophy of the tongue (T. Hodgkin, *Lectures on the Morbid Anatomy of the Serous and Mucous Membranes*, ii. 228, 1840). Other cases have been reported by Blot (*Bull. Soc. de chir. de Par.*, 3 s., ii. 332, 1873), Dolbeau and Félizet (*Bull. gén. de thérap.*, lxxxvii. 442, 1874), E. Martel (*ibid.*, p. 545), Pétrequin (*Gazz. med. ital. lomb.*, 2 s., ii. 169, 1849), and Lannelongue and Ménard (*Affections congénitales*, i. 615, 1891). I have seen a case of unilateral hypertrophy of the tongue without participation of the lip (in a man exhibited by Mr. Wallace at the Edinburgh Medico-Chirurgical Society, November 11, 1903). Sometimes it is the lower lip alone which shows the congenital enlargement (*hypo-macrochelia*, Taruffi). G. Buck (*Trans. Med. Soc. New York*, p. 171, 1872) has reported a case successfully treated by operation; and a hereditary and historical example is found in the Hapsburg or Leopold lip, so characteristic of the descendants of Maximilian I. of Austria and Mary of Burgundy. The Austrian under-lip seems to have come to the Hapsburgs in this way: Frederick III., the father of Maximilian I., was the first of the Hapsburg Kaisers to have it; to quote from Carlyle (*Frederick the Great*, bk. iii. c. 4), " he got it from his mother and bequeathed it in a marked manner; his posterity to this day bearing traces of it; mother's name was Cimburgis (or Cymburga), a Polish princess, Duke of Masovia's daughter," whose almost masculine strength was renowned. Where she got it, I do not know. Cases in medical literature have been reported by M. Eichler (*Diss. inaug.*, Bonn, 1883), by Bloxam (*Brit. Med. Journ.*, i. for 1895, p. 814), and others. The anomaly may be of the nature of a lymphangioma (Billroth), or of primary hypertrophy of the connective tissue, or it may be due to some defect in the development of the first branchial arch. It may be associated with a nævus of the skin of the neighbouring part of the face. An anomaly which is probably closely allied to macrochelia is *dicheilus* (Taruffi) or double lip; it is due to a fold of mucous membrane on the inner aspect of the lip (upper or lower), which gives to it an appearance of duplicity. Another malformation, with resemblances to both the preceding, is *macroglossia.* This congenital hypertrophy of the tongue is in most instances of the nature of a lymphangioma, and is usually bilateral, rarely unilateral. The enlarged organ protrudes from the mouth, producing an appearance which led the early writers to call it "lingua vituli." It has been surgically treated by the removal of a V-shaped portion, and with success. There is a considerable literature upon macroglossia (or megaloglossia), for which the reader is referred to the *Index Catalogue*, xiv. pp. 615–617, Washington, 1893). Unilateral cases were reported by A. Paulicky (*Deutsche mil.-ärztl. Ztschr.*, xi. 212, 1882) and by Wallace; the latter instance I myself examined.

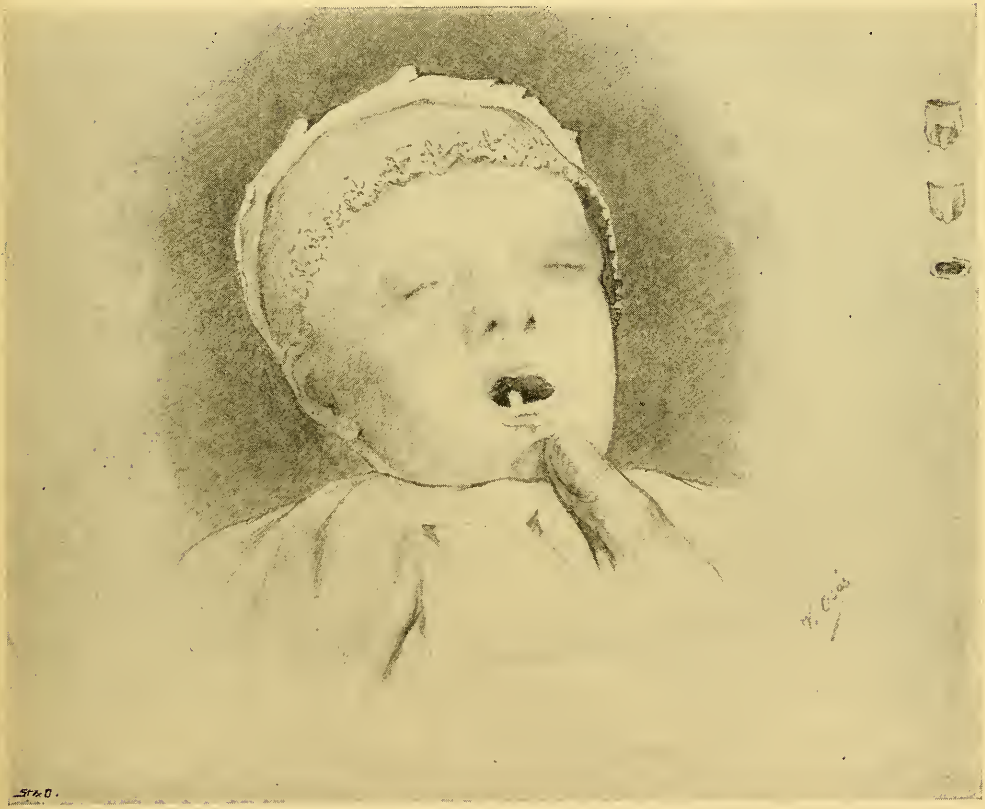


FIG. 64.—Dr. Vargas's Case of Congenital Tooth in Extra-alveolar Dental Sac.

The anomaly may be associated with cystic hygroma of the neck, as in A. Winiwarter's case (*Arch. f. klin. Chir.*, xvi. 655, 1874).

Congenital Teeth.—Teeth, generally incisors, may be present at birth. This antenatal eruption occurs about once in six thousand new-born infants, and I have reported six cases (*Trans. Edinb. Obst. Soc.*, xxi. 181, 1896; xxiii. 112, 1898). In the report which Dr. Vargas of Barcelona sent to me, there was an additional anomaly in the fact that the antenatally cut tooth was in an extra-alveolar dental sac (Fig. 64). Full details of this curious malformation (which is probably fœtal and not embryonic in origin) are to be found in my articles above referred to. It may be associated with hare-lip, cleft palate, tongue-tie, and cyclopia. Irregularities in dental eruption after birth are very common. Occasionally an *additional* incisor *tooth* is present (B. da Costa, *Gaz. med. da Bahia*, xxvi. 308, 1895).

CHAPTER XXII

Merosomatous Terata (*cont.*): Malformations of the Eyes and Nose; Cyclopia: Definition, Historical Note, Clinical History, Morbid Anatomy (Eye, Nasal Apparatus, Facial Bones, Cranium and Brain, Associated Malformations), Comparative Teratology, Teratogenesis, Literature; Cebocephalus; Trigonocephalus; Cryptophthalmus; Anophthalmus; Microphthalmus; Hydrophthalmus; Coloboma of Eyelid; Miscellaneous Malformations of the Eyelids (Microblepharon, Blepharophimosis, Polyblepharon, Ectropion, Entropion, Distichiasis, Epicanthus, Ptosis Congenita); Malformations of the Lachrymal Apparatus, Cornea, Iris, Choroid, Retina, Lens, and Vitreous; Miscellaneous Malformations of the Nose.

In this chapter I shall consider together the teratological states of the eyes and nose. They are very closely associated, indeed in the very characteristic cyclopic monstrosity they are constantly combined. In the succeeding chapter I shall next deal with the anomalies of the ears and lower jaw, for they likewise are frequently associated. At the same time it must be borne in mind that both sets of anomalies may be united in one fœtus (*e.g.* in cyclops hypoagnathus); this simply means that here as elsewhere in Teratology there are connecting links, which, while they disturb the symmetry of classificational systems, are of great value in the understanding of teratogenesis. In this chapter, then, I shall describe first cyclopia, then the nearly allied cebocephalus and trigonocephalus, and then some miscellaneous malformations of the eyes and nose.

Cyclopia.

In cyclopia (or *synopsia*) the two orbits and their contents are more or less completely fused into one. It does not, therefore, simply mean a one-eyed fœtus, in which the singleness of the eye may be due to the absence of its companion organ; but is one in which, by its position as well as by its structure and relations, the eye evidently represents two joined in one. For this reason the synonymous expressions monophthalmus and (less correctly) monoculus are not quite suitable.

Historical Note.—Doubtless the cyclops fœtus is almost as old as the practice of Midwifery itself, and it possibly was the origin (as has been already suggested on p. 84) of the one-eyed Polyphemus of the ancients and his one-eyed subjects, who forged the thunderbolts for Zeus at his "almighty nod" in Sicilian caverns. We read also of the Arimaspi, a one-eyed people, who lived near Arimaspias, a river in Scythia with golden sands; and Lycosthenes in his *Chronicon* (1557) has figured one of them for us (p. 8) with single eye above a normal nose. Licetus (*De Monstris*, p. 133, 1668) reported what was probably a real example of the cyclopic monstrosity, for there was in it a mesial eye with two pupils and a nasal projection or proboscis (which Licetus compared to a penis) above the eye. Licetus also reported a Janus double monster with the same cyclopic deformity, and in the Appendix to the above edition of his work (1668) there is another instance of it in a dicephalic fœtus (p. 296). In the eighteenth century there were not many cases recorded, but that seen by Littre (*Hist. et mém. Acad. roy. d. sc. de Paris*, Ann. 1717, *Mém.*, p. 285, 1719) was noteworthy; in the middle of the face was a single orbit with an eye evidently representing two (it had two optic nerves, retinæ, pupils, lenses, etc., but only one aqueous humour and no choroid); there was no nasal proboscis at all; there were two palpebral fissures in the normal position; there were six digits on the left hand (it is the *right* in the accompanying illustration); and the tongue was adherent to the floor of the mouth, and also to the uvula at its root. It was indeed a curious case, as Littre thought. J. T. Eller's specimen (*Rec. périod. d'obs. de méd., de chir., et pharm.*, vi. 347, 1757) differed from Littre's in being a male and having a nasal proboscis; Mezeray's case (*Hist. Acad. roy. d. sc. de Paris*, Ann. 1761, p. 58, 1763), about which, however, there is some doubt, had two eyes placed one above the other. A great number of observations on cyclopia were made in the nineteenth century, and during the past twenty years marked progress has been achieved in connection with the embryology of the anomaly. Many of the articles and monographs that have appeared between 1800 and the present date will be referred to in the text; but the following are of great importance and may be named here. In addition to valuable contributions in the Text-books on Teratology (such as Saint-Hilaire's, Förster's, Ahlfeld's, Vrolik's, Otto's, Dareste's, and Taruffi's) there have been works by A. Hannover (*Den menneskelige Hjerneskals Bygning ved Cyclopia*, Copenhagen, 1882), O. Larcher (*Dict. encycl. d. sc. méd.*, xxiv. 538, 1880), C. Phisalix (*Journ. de l'anat. et physiol.*, xxv. 67, 1889), A. Bruce (*Proc. Roy. Soc. Edinb.*, xx. 412, 1895), C. Emery (*Anat. Anz.*, viii. 53, 1892–93), and L. Blanc (*Journ. de l'anat. et physiol.*, xxxi. 187, 288, 1895). I have met with two cases (Figs. 18 and 19, pp. 85, 86).

Clinical History.—There is little that requires to be said about the pregnancy which ends in the birth of a cyclops fœtus. It may be accompanied by hydramnios as in the cases reported by H. Vogt (*Norsk. Mag. f. Lægevidensk.*, R. 4, x. 639, 1895), by G. Eustache (*Arch. d. tocol.*, xi. 309, 1884), by W. Craig and J. Symington (*Trans. Med. Chir. Soc. Edinb.*, n.s., v. 178, 1886), and by G. Reguleas (cited by Taruffi, *op. cit.*, viii. 379, 1894). In the last-named case the mother had also frequent attacks of tonsillitis during pregnancy and dropsy of the limbs. Hydramnios, however, is not constant (Hübl, *Centrlbl. f. Gynäk.*, xxii. 21, 1898). Family prevalence may be met with in connection with cyclopia as with anencephaly and other monstrosities;

Caradec (*Compt. rend. Soc. de biol.*, 4 s., iii., pt. 2, 117, 1867), for instance, recorded how a woman gave birth to a female cyclops, then to three well-formed males, and then, seven years later, to a second female cyclops; G. Sapolini (*Ann. univ. di med.*, cciv. 321, 1868), also, related how a woman gave birth to three well-formed male infants, and then to three females, of whom one had hydrocephalus, a second hare-lip and cleft palate, and the third cyclopia. A most remarkable observation was made by R. Ellis (*Trans. Obst. Soc. Lond.*, vii. 160, 1866); it was a case of twins with separate placentæ; one was a female, and had a nasal proboscis and palpebral fissures, and the other was of doubtful sex and had a nasal proboscis and no trace of eyes; the mother had previously given birth to a female infant with cleft palate and imperforate anus. We may take it, then, that this was an instance of dichorionic twins, each with the same type of monstrosity.

The cyclops fœtus does not long survive its birth: it may just breathe (Hübl, *loc. cit.*) or live a few hours, five or six in Blok's case (*Nederl. Tijdschr. v. Geneesk.*, 2 R., xxx., pt. 2, 414, 1894), and seventy-three in Valenti's (*Un caso di ciclopia*, Perugia, 1895). Both in the human subject and among the lower animals (*e.g.* the pig), cyclopia is more common in the female than in the male (Tiedemann, *Ztschr. f. Physiol.*, i. 79, 1842); premature birth has also been noted, and "maternal impressions," as usual, have not been wanting.

Morbid Anatomy.—The essential features of cyclopia are the absence of a well-formed nose in its normal position, the presence of a single eye (often with traces of duplicity in it) in the middle line of the face, and the defective development of the skeleton of the upper and anterior part of the face and of the anterior portion of the brain. The reader has to imagine a developmental failure of the fronto-nasal process, with a consequent approximation and fusion of the two superior maxillary processes, and a disappearance of the parts (nasal fossæ, etc.) which normally lie between them, both in facial region and in the brain. We may, therefore, suitably describe its morbid anatomy under—(1) the eye and its appendages; (2) the nasal organ; (3) the bones of the face, especially those forming the single orbit; (4) the cranium and the brain; and (5) the associated malformations in the head and elsewhere.

(1) *The Eye.* — The eye may be so completely single as to show no trace whatever of duplicity: this was so in my specimen (Fig. 18, p. 85), which was carefully examined for me by Dr. J. V. Paterson, who found only vague traces of duplicity in the retina. On the other hand, all grades of duplicity may be met with, from two eyeballs lying side by side in the single orbit up to the full degree of fusion found in my specimen. These grades were ascribed to different stages of fusion of the two ocular vesicles (S. Rosenstein, *Arch. f. path. Anat.*, vii. 532, 1853). The presence of two eyeballs each of normal size and form and each with its own muscles can hardly be said to have been scientifically demonstrated in cyclopia, but the study of cebocephaly (*q.v.*) would lead us to believe in its possibility. Often, however, the two eyeballs have been found to be

united into one large globe, with a median groove superiorly and inferiorly, with slight atrophy of the contiguous margins, but with no disappearance of any of the essential parts. Each half has its cornea, pupil, lens, and vitreous humour; and the two corneæ are separated by a strip of conjunctiva. The parts (*e.g.* the pupils) lie in the same horizontal plane, with some doubtful exceptions (Mezeray, *loc. cit.*; Gaddi, *Gazz. med. ital. lomb.*, 3 s., vi. 180, 1855). The two corneæ may, in other instances, be fused together, the pupils and the lenses remaining distinct but near together; again, the pupils may be fused into one elliptical opening with the lenses either united or separate; finally, there is the eye single in all its parts, but larger than usual (as in my specimen, Fig. 18). Descriptions of the histology of the eye are few in medical literature; but A. Bruce (*Proc. Roy. Soc. Edinb.*, xx. 417, 1895) found an extraordinarily convoluted appearance of the retina, so that in places it had assumed an almost tubular structure. In correspondence with the state of the eyes is that of the optic nerves: these are separate, or partially united, or completely fused, or rudimentary (Van Duyse, *Arch. d'opht.*, xix. 25, 106, 1899). The muscles also show various anomalies: most commonly the internal recti are absent, sometimes the superior and inferior recti are duplicated; the external recti are generally present; and the obliques are irregular or absent.

It must not, however, be forgotten that the single orbit in cyclopia may contain a more or less *rudimentary* eye. Indeed, there may be no eyeball at all (Caradec, *loc. cit.*; Dumon et Savelli, *Marseille méd.*, xl. 455, 1903); or it may consist of a vesicle covered with the sclerotic, but without lens or cornea. In Van Duyse's case (*loc. cit.*), each pupil showed a coloboma. When the eye is so defective (anophthalmus) the optic nerve is usually little more than an indefinite cord lying on the under surface of the rudimentary brain and advancing no further than the optic foramen (Lannelongue et Ménard, *Affections congénitales*, p. 450, 1891).

Four eyelids are usually found, two upper and two lower, bounding a quadrangular or lozenge-shaped opening; sometimes the two upper or the two lower are fused into one, and then the palpebral fissure is triangular in shape; and there may be other anomalous arrangements. Sometimes the two upper palpebræ do not meet in the middle line; the lower ones usually meet and at their junction there is a single lachrymal caruncula and two papillæ, but there may be only one (Valude et Vassaux, *Arch. d'opht.*, viii. 51, 1888). The eyelids have not their normal structure, and the eye cannot, therefore, be closed, a circumstance which contributes to the peculiar appearance of the cyclops fœtus; there may be a levator palpebræ superioris, or two of them (Lannelongue et Ménard, *op. cit.*, p. 451). There may be a single eyebrow over the cyclopic eye; in other cases there may be two eyebrows in their normal position (Littre, *loc. cit.*). Again, there may be no eyelids round the single eye, but they may be discovered in their normal position. In Valenti's case (*loc. cit.*) there were two contiguous but not continuous palpebral fissures; there was, however, only one orbit.

(2) *The Nasal Apparatus.*—A very characteristic and fairly constant feature of cyclopia is the presence of a nasal proboscis or tube, situated nearly always above the median eye. Gurlt (*op. cit.*, p. 155, 1832) has utilised its presence or absence to make two types of cyclopia—cyclops *rhynchaneus* and cyclops *arhynchus*; while I. Saint-Hilaire (*Histoire*, ii. 383, 1836) has separated two genera of cyclocephalics, one in which the proboscis is present, *rhinocephalus*, and one in which it is not, *cyclocephalus* in the narrow sense. When the proboscis is wanting it has been found that the single eye is also rudimentary or practically absent (anophthalmus), indicating a high degree of absence of development of the mesial structures of the face. Then, as was noted by Lannelongue and Ménard (*op. cit.*, p. 443, 1891), there may be a curious stellate or cruciform depression in the skin of the forehead; under this there is a round opening in the frontal bone, through which the deeper parts of the skin become adherent to the dura mater.

The proboscis, when present, has the following characters. It is situated either between the rudimentary palpebral fissures, or, more commonly, immediately above the single eye-opening in the position of the glabella. In H. Vogt's remarkable case (*loc. cit.*), there was a proboscis above the eye and *another below it*, a circumstance which led him to call the specimen cyclops *dirrhinus* (double-nosed); Taruffi (*op. cit.*, viii. 540, 1894) had an opportunity of examining the fœtus, and confirmed Vogt's description. A sub-orbital proboscis is very rare but not unknown, for Otto (*Seltene Beobachtungen zur Anatomie, Physiologie, und Pathologie gehörig*, Hft. i. 35, 1816) saw it in a cyclopic lamb; but the presence of a supra-orbital and a sub-orbital proboscis in the same case is unique. In form the proboscis is usually cylindrical, but somewhat irregularly cylindrical, a fact which led early writers to compare it to the penis, and later writers (A. Bruce) to a miniature champagne bottle; sometimes it is constricted near its base (*e.g.* in Ullersperger's specimen, *Inaug. Schr.*, Würzburg, 1822). At its free end is a small depression, and a single orifice leading into a small canal or cavity containing mucus and sebaceous material. Sometimes there are two openings; and the space may be divided into two chambers by an incomplete partition. The proboscis may be nearly the length of the normal nose, or it may be little more than the size of a pea (Lannelongue et Ménard, *op. cit.*, p. 493, 1891). It may be pendent over the eye, or project straight out from the face (when it may be found to possess a cartilaginous axis) or be turned up on the forehead (C. Rokitansky, *Lehrbuch der pathologischen Anatomie*, Aufl. 3, iii. 1, 1861). Usually it has a soft consistence, but, as stated above, it may be rigid from the presence of a cartilaginous rod in its interior. Microscopically, it is covered by skin resembling that of the face, under which is adipose tissue, and below that is loose connective tissue containing vessels and striped muscular fibres; in the centre is a tube lined by epithelium and showing racemose glands, and sometimes there is also a rod of cartilage surrounded by fibrous tissue. The nervous supply of the proboscis has not been fully worked out yet; but no traces of olfactory nerves have been found in three specimens investigated by Lannelongue and Ménard (*op. cit.*, p. 444, 1891). This curious organ must be regarded as the soft parts of a nose; the hard parts are wanting, and, through the approximation of the superior maxillæ and the fusion of the orbits, the soft structures are in an abnormal position.

(3) *The Bones of the Face.*—The most striking peculiarity in the facial skeleton is the presence of a single orbit. This cavity, which is usually larger than one orbit and not so large as two would be, is more or less elliptical in shape, and is bounded above by the frontal bones, at the sides by the malars and greater wings of the sphenoid, and inferiorly by the fused orbital plates of the superior maxillæ (without their nasal processes). At the fundus of the orbit is a rounded opening bounded by the malformed lesser wings of the sphenoid, by the sella turcica, and by the frontal bone; through this foramen comes the optic nerve (or nerves). At the sides are the sphenoidal fissures. Several bones are usually entirely absent: these are, the ethmoid, the pre-sphenoid, the vomer, the inferior turbinateds, the nasals, the lachrymals, and the premaxillæ. As a result of their absence, the superior maxillæ and malars are approximated; the former are small in size and lack the nasal processes. The septum of the nose is also wanting. The post-sphenoid and greater wings are generally normal, and so is the lower jaw with the notable exception of the cases of cyclops hypoagnathus. The frontal bones are usually fused together and show a median boss just above the orbit; the single bone, thus resulting, is narrower than usual. Sometimes there is an opening in the frontal bone in the position of the metopic suture. The mode of union of the two superior maxillary bones in the middle line of the face offers some puzzling anatomical problems. The upper lip shows no philtrum, so that, although it appears at first sight to be normal, it must really be regarded as lacking its median part. Lannelongue and Ménard (*op. cit.*, p. 451, 1891) give a mesial section through the skeleton of the face; from it we learn that the two palate bones fuse together into one osseous mass; that in front of this the superior maxillæ are separated only by a thin membrane which intervenes between them from the floor of the orbit to the roof of the mouth, and that anteriorly they (the superior maxillæ) form a single osseous mass which constitutes the alveolar margin. It is thought that the membrane separating the upper maxillæ represents the nasal mucosa (all that is developed of it). The vault of the palate is, therefore, very narrow, but is not fissured; there is a soft palate and behind it is a rounded cul-de-sac into which open the Eustachian tubes. Incisor tooth-germs are usually absent from the upper jaw; but a median (double) incisor attached to a rudimentary intermaxilla has been found. The three upper incisors which have been described (by Hannover, *op. cit.*) are doubtless two canines and a median incisor. It is an interesting and perhaps significant fact that in at least two cases a cyclops fœtus has been born with teeth already cut (Morgagni, *De sedibus*, Epist. xlviii., N. 53, 1761, *English Translation*, B. Alexander, ii. 757, 1769; J. H. M'Lin, *Med. Standard*, xv. 121, 1894).

The muscles of the eyeball have been already described; it may be added that some of those of the face are present (*e.g.*, buccinators, zygomatici, orbicularis oris, levatores menti), while others are absent or defective (muscles of the nose, levator labii superioris, etc.).

(4) *The Cranium and the Brain.*—I have already referred to several characters of the cranium in my description of the orbit and its boundaries, but I may here add some facts relating to the cranium as a whole. The ossification is not as a rule defective, in fact it is common to find the bones hard and the sutures firm and even closed. In my specimen (Fig. 18) the anterior fontanelle was very small in size, but the metopic suture was still present. The dimensions of the whole head are below the normal, and the frontal region specially suffers. The frontal bones (or bone) are small, the occiput is often malformed, and the parietals are fairly normal. The anterior fossa of the cranium is very small, the middle fossa is narrow, and the posterior is not much altered.

The state of the brain is of great importance; in fact, there is a cerebral malformation of as great importance as that of the eyes, orbit, and nose, and as essential to the morbid anatomy of cyclopia. In my specimen (Fig. 18) there was a hydrocephalic sac found occupying the greater part of the cranial cavity with a small brain lying below it; and this has been met with in other cases. The posterior parts of the brain may be fairly normal; thus, the pons, medulla, cerebellum, and corpora quadrigemina may all be easily recognised, and the cerebellum may even be larger than usual. The tentorium cerebelli may be thickened, and is usually displaced upwards and forwards, being attached to the cranium at the level of the lambdoidal suture or even in front of it. The cerebrum is always greatly modified. It may be incompletely divided into two hemispheres, or they may be united throughout; the convolutions and fissures are very slightly marked. The cerebrum leaves the cerebellum exposed. The falx cerebri, as can be imagined, is defective or absent. The olfactory lobes and optic nerves are often wanting; but the other cranial nerves can usually be traced, although the third, fourth, and sixth pair may be very small. In the interior of the cerebrum the corpus callosum, the falx, and the septum lucidum are commonly absent, and the third ventricle forms one cavity with the two lateral ventricles. The optic thalami are fused together, and so may be the crura cerebri. The pituitary body may be recognised, but the pineal may be wanting (A. Bruce, *loc. cit.*). In the spinal cord there is commonly an absence of the descending tracts; in my specimen (Fig. 18, p. 85) there was a small fissure running inwards in the region of the crossed pyramidal tract, where also myelination was defective, but myelination of the direct pyramidal tracts was good. All these changes in the central nervous system point to defective development of the anterior cerebral vesicle.

(5) *Associated Malformations.*—Cyclopia may occur alone as the sole teratological state in a given case; but it is very common for it to be associated with other malformations. Absence of the nasal fossæ and contiguous parts, the presence of the nasal proboscis, and

the peculiar defects of the brain (to which I have referred above) can hardly be called associated malformations, for they are almost as essential as the single orbit and fused eye; but there are other malformations of the face and head which are not so bound up with cyclopia and may yet occur along with it. Some of these teratological states have been used by Saint-Hilaire and others to constitute separate types of monstrosity: the above writer, for instance, gave the name *stomocephalus* to those cases in which, in addition to the cyclopia, there was smallness of the lower jaw and of the mouth and a projection forwards of the superabundant soft parts and skin in the form of a buccal swelling or proboscis. Stomocephalus would seem to be very rare (*vide* I. Saint-Hilaire, *op. cit.*, ii. 403, 1836), but partial or complete absence of the lower jaw with approximation of the external ears in the middle line anteriorly is not so uncommon. One of my specimens of cyclopia (Fig. 18) showed this association with *otocephalus*, as it is called. Further, the name *edocephalus* has been given to the cases in which there is cyclopia, a nasal proboscis, and no mouth; and that of *opocephalus* is assigned to the specimens in which there is neither proboscis nor mouth, but only cyclopia and the fusion of the external ears in the middle line anteriorly. L. Blanc (*Journ. de l'anat. et physiol.*, xxxi. 187, 288, 1895) makes a separate division for these two types under the name *cyclotia*, representing thus the combined nature of the monstrosity. Of otocephalus, edocephalus, and opocephalus I shall have something to say shortly; I refer to them here only as related to cyclopia.

Anencephaly and cephalocele may likewise be associated with cyclopia (*e.g.* in the specimens of Taruffi, *op. cit.*, vi. 372, 1891; of Planchon, *Bull. Soc. anat. de Paris*, xliii. 541, 1868; and of Galloupe, *Boston Med. and Surg. Journ.*, cii. 135, 495, 1880); so may hydrocephalus (Beveridge, *Northumberland and Durham Med. Journ.*, ii. 51, 1894) and hare-lip and spina bifida (Panum, *Nord. med. Ark.*, i. No. 1, 1–25, 1869). Malformations in more distant parts of the body and limbs may also occur: exomphalos (Morgagni, *op. cit.*), umbilical hernia (Saussol, *Gaz. hebd. d. sc. med. de Montpelier*, viii. 458, 1886), abdominal hernia and absence of sternum (J. N. Snively, *Med. and Surg. Reporter*, xxiv. 383, 1871), club-hand (Morgagni, *op. cit.*; G. Reguleas, *Atti d. Accad. Gioenia*, 2 s., iv. 123, 1847), atresia ani (Reguleas, *loc. cit.*), inversion of the viscera (Heuermann, cited by Taruffi, *op. cit.*, viii. 374, 1894), absence of the suprarenal capsules (Riviera, cited by Taruffi), preauricular appendages, absence of right kidney, and uterus unicornis (Stybz, *Arch. de tocol.*, xvii. 392, 1890), polydactyly (Hübl, *loc. cit.*), diaphragmatic hernia (Littre, *loc. cit.*; E. Lacroix, *Tr. med.*, Paris, xiii. 141, 1833), and single umbilical artery (C. Debierre, *Compt. rend. Soc. de biol.*, 8 s., iii. 184, 1886) are among the numerous and varied anomalies that have been recorded.

Comparative Teratology.—Cyclopia is a *comparatively* common monstrosity in the human subject, not so frequent as anencephaly, but yet fairly common. Among the lower animals it has a surprising frequency, and indeed it seems to take the place with them that anencephaly holds in the human subject. Hannover (*op. cit.*)

collected together the records of cyclopia in man and in the lower animals, and obtained the following table:—

Human subject	103
Calves	30
Lambs	51
Pigs	130
Puppies	22
Kittens	12
Foals	10
Kids	9
Rabbits	3
Deer	1
	268

C. Taruffi (*op. cit.*, vi. 433, 1891) collected 43 cases in the human subject (not including 18 instances of cyclops hypoagnathus), 10 in calves, 28 in lambs, 47 in pigs, 11 in puppies, 7 in kids, 7 in kittens, 12 in foals, and 1 in the ass—a total of 166 cases, including 123 in the lower animals. It also has been noted in birds (chicken, goose, dove, duck), and in fish (salmon). Symington and Woodhead (*Proc. Roy. Phys. Soc. Edinb.*, ix. pt. i., 268, 1886) described 10 specimens of cyclopia, 3 in the pig, 2 in puppies, and 1 each in the human subject, kitten, calf, lamb, and sheep; they add that Brotherston had met with about thirty cyclopic lambs, the offspring of one ram. We do not understand the meaning of these facts in Comparative Teratology, although it is evident they must have a significance. The morbid anatomy of cyclopia in the lower animals, especially as produced artificially in chicks, has many interesting features, into which it is impossible for me to enter; but I may refer here to Lavocat's observation (*Rev. vétérinaire*, Toulouse, x. 233, 1885). It was that of a lamb which had neither median eye nor median orbit, and there was also absence of the olfactory apparatus and premaxilla. Lavocat proposed to call it *ophthalmocephalus* and to separate it from cyclopia; and Taruffi agrees with him in the latter point, but would call it *atrochius* (without orbit) *arhynchus* (without nose), which is etymologically correct although unfamiliar (*op. cit.*, vi. 379, 1891).

Teratogenesis.—With regard to the origin and meaning of cyclopia much has been written of recent years, and the reader is directed to Etienne Rabaud's fine series of monographs (*Journ. de l'anat. et physiol.*, xxxvii. 345, 575, 1901; xxxviii. 35, 282, 510, 1902) for a perfect mine of information on these difficult matters. The theories that have been adduced to explain its origin are by this time familiar to the reader; they are those known as the traumatic, the nosological (or pathological), the amniotic, and the embryological. I need not enter into detail regarding these theories, for their general principles, stated in an earlier part of this volume, apply also in such a special case as cyclopia. The traumatic or mechanical theory was advanced in the eighteenth century, and held to some extent also in the nineteenth; the idea of the two eyes being more or less completely fused by some compressing force was, however, a very vague one till Dareste and others gave it definiteness by alleging that the head fold of the amnion was the compressing agent. Nosological theories may be said still to prevail in many observers' minds: thus A. Bruce (*loc. cit.*) regards a limited pachy- and lepto-meningitis as a separate, or at least contributing, cause of cyclopia; and other writers have ascribed the changes to hydrocephalus. It has, however, been shown already in the discussion of the nosological theory in teratogenesis that the idea of diseases as the causes of monstrosities is hardly tenable in the light of the chronology of antenatal processes. Panum (*loc. cit.*), for instance, met with cyclopia in an embryo of six weeks, at which early date it is scarcely possible to conceive of the occurrence of diseases in the meninges or lining membrane of the ventricles.

The amniotic theory was strongly stated by Dareste first in 1877 and later in his *Production artificielle des monstruosités* (2nd edit., 373, 1891). He regarded cyclopia as due to amniotic compression which arrested the development of the anterior cerebral vesicle; there is then premature closure of the anterior wall of the first cerebral vesicle, the parts of the optic vesicles which form the two retinæ unite in the middle line instead of being separated from each other, and so interfere with the formation of the cerebral hemispheres and the parts formed from them. Rabaud (*loc. cit.*), a pupil of Dareste, has recently pointed out that in artificially produced cyclopia in chicks in which there is evidence of amniotic compression, the morbid changes found are not those of true cyclopia but rather of states resembling cebocephaly (approximation of the eyes). Rabaud thinks there is only an external resemblance to the cyclopic state in these pressure-produced monstrous chicks.

Apart from questions as to the cause of the disturbed ontogeny that leads to cyclopia, there is an almost complete agreement among writers on the subject that the monstrosity is the result of an arrested development. There is some difference of opinion, however, as to the primary localisation of the arrest. Dareste is strongly of opinion that the dominating factor is the defective state of the brain, and that the facial and other malformations follow upon this. There is an arrest of the ontogeny of the anterior cerebral vesicle, the groove from which it normally forms closing too early and so bringing together the parts from which the retinæ of the two eyes are formed and leading to their fusion. In a similar manner the single condition of the anterior part of the brain is held to determine the condition of the nose and face. There are, however, some difficulties in accepting this theory, for it does not seem that the development of the face is always determined by that of the brain, an obvious exception being anencephaly, in which, of course, there is disturbance of the ontogeny of the central nervous system often with no considerable facial deformities at all. I may mention here that all are not agreed that the primary defect lies in the nervous system, Hannover (*op. cit.*), for instance, ascribing it to imperfect formation of the prechordial part of the base of the skull; but this opinion is exceptional, and it may be said that the importance of the cerebral defect is generally recognised. Rabaud (*loc. cit.*) is inclined to regard the cyclopic differentiation as a special evolution rather than as an arrested development, as a new procedure in ontogenesis which entails novel correlations in development ("origine adaptative"), and is determined by an external agency, the nature of which is unknown and about which we are unable at present to advance a hypothesis. There is much that is uncertain about the teratogenesis of cyclopia, but that the explanation is to be found in Embryology is a clearly established deduction from the data we possess.

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Cebocephalus.

The monstrosity which is known as cebocephalus has by some teratologists (*e.g.* Saint-Hilaire) been placed with cyclopia proper in the family of the cyclocephalians ; but it is preferable to regard it as a type by itself, although it undoubtedly is closely related to cyclopia, and may even be regarded as an incomplete form of it. Inasmuch, however, as there are two orbits and not one, it fails to fulfil the requirements of the definition of cyclopia. In cebocephalus the two orbits are approximated, and, in consequence of this, the nose is deformed and the whole face diminished in size. The expression of the face is ape-like, hence the use of the term cebocephalus (κῆβος, ape, κεφαλή, head) has some appropriateness. This type is comparatively rare, for Taruffi only succeeded in collecting twenty-six case-records ; but it is possible that some instances have been reported under malformations of the nose, for the nasal deformity is often more evident than the ocular.

I have not myself seen a specimen of cebocephalus, but in 1899 Professor A. R. Simpson handed to me a letter he had received from Dr. G. T. Smith of New Brunswick, containing the description of a fœtus which I have little doubt was an instance of this teratological type. It was a female child, the product of the second pregnancy of a strong, healthy woman, thirty-four years of age ; the first pregnancy, eight years previously, had ended in the birth of a normal infant. The labour was full time and there was hydramnios. The child lived twenty minutes only. The ears and mouth were normal ; the eyes were absent, but there was a slight depression in the position of the right eye and a superficial slit, $\frac{1}{3}$ inch long, where the left eye should be. The nose was a tube, arising between the two ocular depressions, and standing straight out from the face ; it was about $\frac{3}{4}$ inch long, quite flexible, and had two openings at its free end. The right foot was very narrow, appearing to consist of one metatarsal bone, and it ended in one well-marked digit (with a nail) the same length as the toes of the left foot (which was normal). The right hand was normal, but the left carried only four perfect digits, with a rounded soft mass, the size of a cherry, springing from the base of the metacarpal bone, to which it was attached by a pedicle and carried a nail. The placenta and cord seemed normal.

Dr. Smith was not able to dissect the child, and so no information is available as to the state of the orbits, but I think it may be grouped as a specimen of cebocephalus in which the nasal deformity took the form of a proboscis such as is often seen in cyclopia. For this type Isidore Geoffrey Saint-Hilaire created a special genus bearing the name *Ethmocephalus* (*Histoire*, ii. 378, 1836) ; but there is no special appropriateness therein. In other cases the nose may simply be flattened, and have one opening (without any septum, and often rather narrow), or more rarely two apertures. The mouth is generally small, but the lower jaw may be quite normal. Commonly there is closure of the frontal (metopic) suture, and the frontal eminences form one median projection. The whole face is smaller, and the palpebral slits are oblique, their internal angles being lower than the external.

The essential feature, however, is the approximation of the orbits. This is due to the absence (or incomplete development) of certain bones, including the ethmoid, the nasals, the superior turbinated, the lachrymals, and the vomer. The premaxillæ may also be small in size. The inter-orbital space is small in extent, the orbits are wide and high, and the optic foramina large.

The brain shows the same malformations as in cyclopia: there is absence of the olfactory nerves, the corpus callosum, and the septum lucidum; the anterior lobes are malformed, and indeed the whole cerebrum may be single and small in size, although in other cases there is the indication of two hemispheres with a median sulcus; the convolutions are slightly marked; and the lateral ventricles communicate freely and widely with the third.

Associated malformations are comparatively common. There was an adhesion of the placental amnion in A. Charvet's case (*Cébocéphalie*, Grenoble, 1874); bilateral labial, alveolar, and palatal fissures in Fridolin's cases (*Arch. f. path. Anat.*, civ. 158, 1886; cxii. 536, 1888); absence of the premaxillæ (C. Hecker and L. Buhl, *Monatschr. f. Geburtsk. u. Frauenkr.*, xxxi. 430, 1868; H. Kundrat, *Arhinencephalie*, Graz, 1882), absence of the eyeballs in C. Renner's case (*Diss. inaug.*, Halle, 1889), polydactyly and double uterus and vagina (Renner, *op. cit.*), and there were defects of the left hand and right foot in Smith's case (above related).

The teratogenesis of cebocephalus need not be specially considered, for what has been said regarding cyclopia may be applied here. Its comparative teratology also closely resembles that of cyclopia, for it is more common in the pig than in any other animal. Owing to peculiarities in the regional anatomy of the face in animals the approximation of the orbits is not very striking, and, therefore, it is not surprising that the maxillary anomaly (*brachyrhynchus*) is the feature that specially appealed to the veterinary pathologists who met with instances of it (*e.g.* Gurlt).

Trigonocephalus.

Trigonocephalus (triangular head) or *oocephalus* (egg-shaped head) is a somewhat incompletely differentiated teratological type; indeed it may be said to be a cranial character met with in both cebocephalus and cyclopia. At the same time it may occur apart from both these monstrosities (H. Welcker, *Ueber zwei seltnere Difformitäten des menschlichen Schädels*, Halle, 1863). Although rare, Taruffi (*op. cit.*, vi. 358, 1891) has succeeded in collecting together nineteen instances of it from literature, including three cases described by Hanns Kundrat in his admirable monograph (*Arhinencephalie als typische Art von Missbildung*, Graz, 1882). The anterior part of the cranium is pointed or triangular, the apex of the triangle being the middle point of the forehead. There is premature synostosis of the two halves of the frontal bone (J. Fridolin, *Arch. f. path. Anat.*, civ. 156, 1886), occurring according to O. Küstner (*Arch. f. path. Anat.*, lxxxiii. 58, 1881) at the twentieth week of antenatal life. The eyes are obliquely placed, their inner angles being lower than their outer; and in some instances the orbits are approximated. The state of the brain very closely resembles that found in cebocephalus and in cyclopia: it is arhinencephalic, to use Kundrat's word. The olfactory nerves are often wanting, and the anterior part of the cerebrum is single. There may also be hydrocephalus (as in one of Kundrat's cases). Other associated malformations are microphthalmus, cleft palate, double hare-lip, omphalocele, and a perforate condition of the ventricular septum of the heart. The premaxillæ may be small in size. The malformation is not incompatible with postnatal life: one of Küstner's cases was two years of age. It is to be regarded as a slight degree of the same series of changes as produce cebocephalus and cyclopia; and it is probably due to the same cause, whatever that may be.

Malformations of the Eyes.

Many malformations of the eyes exist, as every student of Ophthalmology knows; but I can only give them a passing notice here. A book might easily be written, instead of part of a chapter, upon the structural anomalies of the eye and its appendages.[1] The multiplicity of its malformations is fully explained by the complexity of the development of the eye.

Cryptophthalmus.

In this type of malformation the skin passes without a break from the forehead on to the cheek, and the openings of the orbits are thus quite closed in. The term *cryptophthalmus* has been preferred by recent writers to that of *ablepharon*. It is not to be confused with adhesion of the eyelids (*ankyloblepharon*), which is hardly a malformation, for it occurs comparatively late in fœtal life, and is possibly due to antenatal disease (*blepharitis*); it must also be distinguished from adhesion of the palpebral and ocular conjunctival surfaces (*symblepharon*). A typical instance of cryptophthalmus was reported by W. Zehender (*Eine Missgeburt mit hautüberwachsenen Augen*, Rostock, 1872), with a detailed description of the eyes by Manz. The child, a female with anomalies of the external genitals, died at the age of nine months. There were no eyebrows and no trace of a palpebral fissure; only the skin covering the orbits was thin and devoid of fat. There was also a small umbilical hernia and syndactyly of the hands and feet. The optic nerves were present. The eyes were discovered in the orbits at the necropsy: the conjunctival sac was absent; the lens and iris of the right eye were absent, the ciliary processes and bodies were rudimentary, but the cornea was represented; the left eye was distinctly smaller than the right, and had a normal choroid and retina. Another typical case was put on record by Van Duyse (*Contribution à l'étude du cryptophtalmos*, Bruxelles, 1899; *Belgique méd.*, vi. 705, 1899), with a good dissection and numerous drawings of the microscopic characters of the eyes. Yet other cases have been described by Fuchs (*Wien. med. Blätt.*, xii. 215, 1889), H. Otto (*Wien. klin. Wchnschr.*, vi. 883, 1893), and S. Karman (*Orvosi hetil.*, xxxviii. 139, 1894; *Arch. f. Kinderhlk.*, xviii. 206, 1894–95), and in the lower animals by L. Bach (*Arch. f. Augenh.*, xxxii. 16, 1895–96), by Van Duyse (*op. cit.*), and G. de Grandmont (*Arch. d'opht.*, xiii. 742, 1893). Taruffi (*op. cit.*, vi. 440, 1891) also refers to cases by Chiari (a female fœtus with hare-lip, syndactyly, facial asymmetry, atresia of the larynx, and urino-genital defects) and Coen (a fœtus with absence of the kidneys and uterus). The eyeballs would appear sometimes to show unmistakable signs of inflammation, the lachrymal glands may be absent, there is often a displacement of the parts of the eye, and the lens may be present but in a degenerated state. It has, therefore, been maintained that inflammation of the eyes in antenatal life is the causal factor in cryptophthalmus, and that an amniotic adhesion may be instrumental in inducing it; fusion of the lids would follow. On the other hand, it is possible that there is in this morbid state a lack of development of the lids, and that the other changes are secondary (*i.e.* a teratological and not a nosological condition). The matter cannot at present be decided; but it may be that, after all, cryptophthalmus differs from ankyloblepharon only in the earlier date in antenatal life at which it is initiated. The changes in the eyeballs do not hold out much hope of successful operative interference.

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[1] Since this sentence was penned Professor Van Duyse's work, *Elements d'embryologie et de tératologie de l'œil*, has been published (1904).

Anophthalmus (Anopsia).

Absence of the eyeball either on one side only (*monophthalmus*) or on both (*anophthalmus*) is not so rare as cryptophthalmus. I was able to examine a case some years ago, which was brought under my notice by Dr. Bunting. It was that of a female child of five months. The mother, age thirty-nine, had had eight pregnancies, and the child with monophthalmus was the product of the fifth. The first three infants died, two of them soon after birth and the third before birth; the second and third were born at the seventh month. The other children were full time and were all alive. The father, age thirty-nine, was suffering from eye trouble (tertiary syphilis ?) when this child was conceived. It was the right eye that was absent. The right rima palpebrarum measured less than ½ inch (1 cm.) in length, while the left was nearly an inch (2·3 cm.), and the opening of the former was nearer the middle line. It was provided with some eyelashes, and tears came from it. The right ear was a little larger than the left, and there was cranial asymmetry, the right side of the head showing very little parietal prominence. There was hardly any eyebrow on the right side, and some entropion was noted. The left eye was dark grey in colour and reacted well to light. The hands and feet and the genitals were well formed.

This case (Fig. 65) may be taken as a typical instance of unilateral anophthalmus. It is apparently rarer than the bilateral variety. The optic nerves may be absent or atrophic, and the atrophy may extend to the optic chiasma and corpora quadrigemina. The contents of the orbit may be simply connective tissue, or the muscles of the absent eyeball may be discovered. The lachrymal apparatus may be perfect, or the carunculæ defective. The eyelids may also be complete and capable of movement; the palpebral slit is usually small, and there may be adhesion of the margins of the lids (ankyloblepharon) and some degree of entropion. Associated malformations have been met with: club hands and feet, cleft palate, polydactyly, bifid tongue, hare-lip, cranial asymmetry, and preauricular appendages. The malformation, in itself, does not interfere with postnatal life. The mother of Ramage's patient (*Brit. Med. Journ.*, i. for 1894, p. 681) had convergent strabismus. It has been met with in animals (*perocephalus anommatus,* Gurlt).

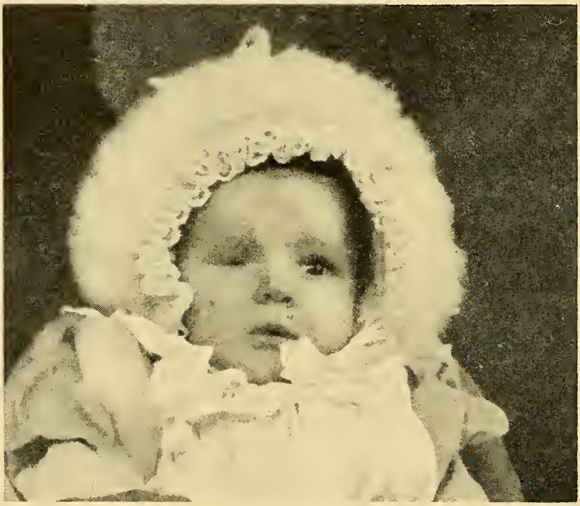

Fig. 65.—Case of Unilateral Anophthalmus.

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Microphthalmus.

Under the name *microphthalmus* have been grouped together many cases of diminution in the size of the eye, varying in degree from those in which the smallness was slight to those in which the eyeball was not larger than a pea. There can hardly be drawn any line dividing marked microphthalmus from anophthalmus; indeed it has been believed by some that the latter malformation is only the last degree of the former. At any rate the two malformations have been met with in the same subject (E. T. Collins, *Ophth. Hosp. Rep.*, Lond., xi. 429, 1887).

Microphthalmus is more often bilateral than unilateral, but even when bilateral it may be of different degree. There may be no other defect than smallness in size; but on the other hand malformations of the eye are very common. In a case which I examined in September 1895 (it was brought under my notice by Dr. Oliphant Nicholson, then of Kirkcaldy) there was microphthalmus and aniridia of the right eye and coloboma of the iris of the left. Other associated malformations are corneal defects; coloboma of the vitreous, of the choroid, and of the optic nerve; absence of the lens, iris, and ciliary bodies; retinal and orbital anomalies; blepharophimosis and blepharoptosis; and cysts of the lower eyelid or in the interior of the orbit. Microphthalmus occurs in the lower animals, and received from Gurlt the name of *nanocephalus micrommatus* (*Lehrbuch der path. Anat. der Haus-Säugethiere*, ii. 109, 1832).

Like so many other malformations, microphthalmus may show family prevalence (A. Gescheidt, *Ztschr. f. d. Ophth.*, ii. 257, 1832); it may also affect a father and his sons (P. Gradenigo, *Giorn. veneto di sc. med.*, 3 s., iii. 703, 1865), and may even be transmitted to the third generation (G. Mayerhausen, *Centrlbl. f. prakt. Augenh.*, vi. 97, 1882). Other ocular diseases and anomalies may be found in the relatives of individuals suffering from microphthalmus. Some interesting experiments upon animals by J. Samelsohn (*Centrlbl. f. d. med. Wissensch.*, xviii. 305, 322, 1880) would almost seem to show that injuries inflicted upon the eyes of the parent might induce microphthalmus in the offspring; but there is grave doubt whether this theory can be accepted.

There are two chief theories regarding the origin of microphthalmus, and they apply also to anophthalmus. The reader, doubtless, has already guessed that according to some authors the changes are produced by diseases (*e.g.* fœtal choroiditis, P. Caudron, *Rev. gén. d'opht.*, vi. 97, 1887) or by cystic growths, while others look upon them as arrested developments (want of closure of ocular vesicle, etc.). The greater probability rests with the second theory.

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Hydrophthalmus Congenitus.

If not actually an embryonic malformation of the eye it would seem that hydrophthalmus congenitus is generally the result of such a malformation. Under this name or under the synonymous terms, *megalophthalmus*, *buphthalmus* (ox-eye), and *congenital glaucoma*, a considerable number of cases have been reported in which the eyeball is enlarged and has its tension increased. The front of the eyeball is more globular than normal; the sclerotic is thinned with the pigment shining through and giving it a bluish appearance; the cornea is enlarged; the anterior chamber is, in most instances, deep, but may on the other hand be absent through the iris being in contact with the cornea; and the optic nerve is cupped. The obstruction to the circulation in the eye would appear to be due to a want of separation of the iris from the cornea in the region of the ligamentum pectinatum; a stretching of such an adhesion may occur as life goes on and so a spontaneous cure take place. In E. von Hippel's case (*Arch. f. Ophth.*, xliii. 3 Abth., 539, 1897) there were signs of former irido-cyclitis and parenchymatous keratitis; the lens was very small; and there was nearly complete absence of Schlemm's canal. I may add here some references to this interesting ocular anomaly, which lies on the border-line between the embryonic malformations and the fœtal diseases. F. Arnold, *Beitr. z. Augenh.*, 216, 1890–91; F. R. Cross, *Trans. Ophth. Soc. Unit. Kingdom*, xvi. 340, 1895–96; Dürr and Schlegtendal, *Arch. f. Ophth.*, xxxv. 2 Abth., 88, 1889; M. Dufour, *Rec. d'ophth.*, 3 s., iii. 674, 1881; C. Gallenga, *Ann. di ottal.*, xiv. 322, 1885–86; C. Grahamer, *Arch f. Ophth.*, xxx. 3 Abth., 265, 1884; O. Hasse, *Diss. inaug.*, Strassburg, 1892; Manz, *Amtl. Ber. ü. d. Versamml. deutsch. Naturf. u. Aerzte*, lvi. 252, 1884; R. Schirmer, *Klin. Monatsbl. f. Augenh.*, ix. 250, 1871; C. Schœnemann, *Arch. f. Augenh.*, xlii. 174, 1900; and F. Vianey, *Echo méd.*, Toulouse, 2 s., xv. 89, 1901.

Coloboma of Eyelid.

By *Blepharocoloboma* or *Coloboma of the Eyelid* is meant a vertical fissure or defect of one or other or both eyelids. It is comparatively common, and it may occur in association with facial fissures (*q.v.*) or alone. I have met with several instances of it (Figs. 25, 26, 30), and Taruffi collected from literature forty-six cases in which it occurred apart from fissures of the cheek (*op. cit.*, vi. 456, 1891). When it is present alone it is more common in the upper than in the lower eyelid; but if the cases associated with genal clefts be included there is no marked disproportion between the two lids. It usually involves the whole thickness of the lid; it varies in size from a small notch in the palbebral margin to a wide triangular or quadrangular cleft; in the lower eyelid it usually has the shape of a V, and that of an inverted V in the upper. Only one lid may be affected; but two, three, and even all the four have been found fissured. The coloboma generally is situated towards the inner side of the middle line of the eyelid, less commonly in the middle line, and rarely in the outer half. The margins of the cleft may be smooth or provided with eyelashes, white as if cicatrised or red, and sometimes a membranous band (amniotic?) passes to the eyeball to be attached to the cornea. Sometimes a dermoid tumour of the eyeball has been found lying in the cleft. Among the associated malformations are facial, genal, nasal, and labial fissures, defect in the eyebrow or in the skin of the forehead, symblepharon, microphthalmus, coloboma of the iris and choroid, and preauricular appendages. The teratogenesis of coloboma palpebræ is difficult to understand. It is not a simple arrest, for there does not seem to be any stage in ontogenesis to which it corresponds, although when it is combined with a genal fissure it may represent an extension of its upper end. It is probable that it is due to an adhesion of the amnion to the eyeball which prevents the growth of the lid at that part. There are difficulties in the way of a complete acceptance of this view also, but it is supported by a number of facts, and in one at least of my cases an amniotic band was actually present.

In addition to the numerous references given by Taruffi (*op. cit.*) I may name the following:—L. A. W. Alleman, *Ann. Ophth.*, St. Louis, vii. 183, 1898; A. Berthaud, *Lyon méd.*, lxxiii. 288, 1893; A. Brinkmann, *Diss. inaug.*, München, 1887; M. Capel, *Sperimentale*, Ann. xlvi. 229, 1892; G. Cowell, *Trans. Ophth. Soc. Unit. Kingdom*, xi. 214, 1890–91; H. Dor, *Rev. gén. d'opht.*, vii. 529, 1888; W. Goldzieher, *Centrlbl. f. prakt. Augenh.*, xx. 359, 1896; J. Hoppe, *Arch. f. Ophth.*, xxxix. 307, 1893; *Arch. f. Augenh.*, xxxvii. 354, 1898; J. Krischewsky, *Diss. inaug.*, Würzburg, 1894; H. Juler, *Trans. Ophth. Soc. Unit. Kingdom*, xii. 171, 1891–92; W. Lang, *ibid.*, vi. 488, 1885–86; J. Nicolin, *Thèse*, Lyon, 1888; Osio, *Rev. de enferm. de niños*, i. 115, 1883; E. Owen, *Trans. Med. Soc. Lond.*, xiii. 204, 1889–90; Schanz, *Deutsche med. Wchnschr.*, xxiv. 288, 1898; S. Snell, *Trans. Ophth. Soc. Unit. Kingdom*, iv. 348, 1883–84; Zeilendorf, *Wien. klin. Wchnschr.*, vii. 729, 1894.

Miscellaneous Malformations of the Eyelids.

Complete absence of the eyelids (true *ablepharon*) is almost unknown save in association with other grave defects and monstrosities; this condition is not to be confounded with cryptophthalmus in which the eyelids are absent only in the sense that they are represented by a continuous cutaneous covering. Congenital shortness of the eyelids, especially of the upper ones, is known as *microblepharon*; the palpebral fissure on this account is incompletely closed (*lagophthalmus* or "hare-eyed," this animal being supposed to be unable completely to close its eyes). *Blepharophimosis*, or smallness of the palpebral aperture, is usually associated with and caused by microphthalmus and anophthalmus.

A supernumerary eyelid (*polyblepharon*) has sometimes been met with. To an accessory (semilunar) fold of scleral conjunctiva on the nasal side of the eye the name of third eyelid (palpebra tertia) or membrana nictitans has been given; it is supposed to represent the structure which is found in a fully developed form in birds and some reptiles. Another sort of supernumerary eyelid in the human subject has also been described: it is a conjunctival fold at the outer angle of the eye, and may be regarded as a fourth eyelid (palpebra quarta). Case-records have been published by Dubois (*Ann. d'ocul.*, xxxiv. 268, 1855), Fano (*ibid.*, xlix. 23, 1863), and J. Larcher (*Thèse*, Paris, 1889). Congenital *ectropion* and *entropion* have been met with, but are very rare; the former is associated with fœtal ichthyosis (*vide* Vol. I. p. 308); and the latter is peculiar in that the inturned eyelashes do not rub against the cornea with their points, but laterally, and so give rise to little irritation. A second row of eyelashes (*distichiasis*) has been found.

Epicanthus is a cutaneous fold found sometimes covering either the inner or outer canthus or angle of the eye. The internal form is generally due to a slight nasal defect, and is present almost constantly in the Mongolian race. It gives to the eye the appearance of convergent strabismus, and it disappears when the skin of the root of the nose is pinched up. It may occur, but rarely, over the outer angle of the eye (Sichel, *Ann. d'ocul.*, xxvi. 29, 1851). Various operations have been devised for the removal of the deformity (F. A. von Ammon, *Ztschr. f. d. Ophth.*, i. 533, 1830; Carron du Villards, *Bull. gén. de thérap.*, xv. 45, 1838; W. Fröbelius, *Med. Ztg. Russlands*, iv. 335, 1847; *St. Petersb. Med. Ztschr.*, i. 322, 1861; H. H. Walton, *Med. Times and Gaz.*, n.s., vii. 218, 1853; H. Knapp, *Arch. Ophth. and Otol.*, iii. 48, 1873; E. Berger, *Arch. d'opht.*, xviii. 453, 1898; H. Kuhnt, *Ztschr. f. Augenh.*, ii. for 1899, 169).

Associated with epicanthus it is not uncommon to find a drooping of the upper eyelid or *ptosis congenita*; but this anomaly may also exist apart from an epicanthic fold. I have recently met with an instance of it in a mother and infant in the Royal Maternity Hospital, Edinburgh; it was the right eye in both, and it was stated that the mother's mother had the same anomaly. I have also in my possession the photograph of a little girl with bilateral ptosis palpebrarum, which Dr. J. Crawford Dunlop gave me. It may be associated with microphthalmus and coloboma as well as with epicanthus. It is commonly due to developmental defects in the muscles; it may, as in my case, be hereditary, and it may also show family prevalence (Dujardin, *Journ. d. sc. méd. de Lille*, xvii. 561, 1894). The bilateral form is more common than the unilateral. Various operations have been attempted for the relief of the deformity due to blepharoptosis. Freeland Fergus (*Brit. Med. Journ.*, i. for 1901, 762), for instance, makes a horizontal incision in the position of the eyebrow, dissects out a vertical band of the tendon and fascia of the occipito-frontalis, and secures it to the upper eyelid as near as possible to its margin. Various articles dealing with congenital ptosis have appeared; the following may be enumerated:—G. Ahlström, *Beitr. z. Augenh.*, xvi. 51, 1894; V. Caudron, *Rev. gén. d'opht.*, iv. 241, 1885; A. Dehenne, *Bull. et mém. Soc. franç. d'opht.*, ix. 83, 1891; A. von Graefe, *Arch. f. Ophth.*, ix. 2 Abth., 57, 1863; R. M. Gunn, *Trans. Ophth. Soc. Unit. Kingdom*, iii. 283, 1882–83; C. A. Hall, *Amer. Journ. Med. Sc.*, n.s., xii. 143, 1846; E. B. Heckel, *Internat. Clin.*, 4 s., i. 307, 1894; J. H. Jackson, *Lancet*, i. for 1894, p. 11; V. Miller, *Brit. Med. Journ.*, i. for 1898, p. 1259; F. Mitry, *Thèse*, Paris, 1885; E. Pereyra, *Sperimentale*, xlvii. 384, 1881; T. Proskauer, *Centrlbl. f. prakt. Augenh.*, xv. 97, 1891; R. Rampoldi, *Ann. di ottal.*, xiv. 49, 1885–86; xv. 54, 1886–87; E. Siemerling, *Arch. f. Psychiat.*, xxiii. 764, 1891–92; W. N. Sinclair, *Ophth. Rev.*, xii. 80, 1893; Steinheim, *Klin. Monatsbl. f. Augenh.*, xv. 99, 1877; F. Tartuferi, *Riv. clin. di Bologna*, 2 s., ix. 337, 1879; Thomas, *Johns Hopkins Hosp. Bull.*, vi. 164, 1895; S. Watson, *Brit. Med. Journ.*, i. for 1869, p. 122. For references to the various operations of Panas, Wolff, Kunn, and Mules, *vide* the *Index Catalogue*, 2 s., v. 410, 1900.

Malformations of the Lachrymal Apparatus.

Malformations of the lachrymal apparatus (gland, duct, sac, canaliculi) are usually associated with other grave ocular defects (cryptophthalmus, anophthalmus, etc.); rarely do they occur alone. Perhaps, however, *absence* of one gland is implied by unilateral absence of tears (A. S. Morton, *Trans. Ophth. Soc. United Kingdom*, iv. 350, 1883–84); complete absence of tears has also been recorded (J. Solomon, *Gaz. d. hôp.*, xxviii. 22, 1855), and may mean bilateral absence of the gland; on the other hand, these anomalies may be purely functional. Instances of *fistula* of the lachrymal sac (due to incomplete closure of the embryonic groove) have been recorded (W. Rider, *Arch. Ophth.*, New York, xiii. 263, 1884; J. Dunn, *Arch. Ophth.*, xxiv. 251, 1895); fistula of one or other of the canaliculi has also been noted (Behr, *Klin. Ztschr. f. Chir. u. Augenh.*, i. 456, 1836–37). There may be *absence* or *imperforation* of one or more of the puncta lacrymalia (S. M. Burnett, *Arch. Ophth.*, xiii. 53, 1884; E. Emmert, *Arch. f. Augenh. u. Ohrenh.*, v. 399, 1876; Magnus, *Klin. Monatsbl. f. Augenh.*, xiii. 199, 1875); on the other hand, supernumerary puncta have been met with (C. E. Fitzgerald, *Ophth. Hosp. Rep.*, Lond., viii. 427, 1874–76; A. von Graefe, *Arch. f. Ophth.*, i. 1 Abth., 288, 1854–55; F. Ponti, *Gior. d'oftal. ital.*, ii. 97, 1859; F. Raab, *Klin. Monatsbl. f. Augenh.*, xiii. 331, 1875). It may also be noted that the lachrymal caruncle may be the site of dermoid growths.

Malformations of the Cornea.

Complete congenital *opacity* of the cornea may be found in association with both hydrophthalmus and microphthalmus, and is then probably due to an anomalous arrangement of the constituent layers of the membrane (A. Tepljaschin, *Arch. Ophth.*, xxvi. 64, 1897). Localised opacities are sometimes of a dense white character and may be near the corneal margin, where they may form isolated areas or constitute a ring ("arcus juvenilis," "macula arcuata"). Many instances of congenital corneal opacity have been reported, among which may be mentioned those by E. Fuchs (*Wien. med. Bl.*, xvii. 197, 1894), by R. Hilbert (*Arch. f. path. Anat.*, cxxxi. 182, 1893), by H. Moulton (*Journ. Amer. Med. Assoc.*, xxx. 247, 1898), by F. Rückert (*Ztschr. f. vergleich. Augenh.*, iii. 102, 1885), by J. Santos Fernandez (*Trans. Amer. Ass. Obst. and Gynec.*, v. 424, 1893), and by O. Wernicke (*Ann. d'ocul.*, cxvi. 278, 1896). Congenital clouding of the cornea in two sisters was recorded by R. L. Randolph (*Amer. Journ. Med. Sc.*, n.s., xcvi. 570, 1888), and in mother and son by C. A. Oliver (*Ophth. Rev.*, xi. 349, 1892). G. Saltini's record of three brothers suffering from the anomaly was remarkable (*Boll. d'ocul.*, x. 67, 1888); he ascribed the corneal clouding to fœtal interstitial keratitis, and possibly the condition is a fœtal disease rather than an embryonic malformation. Of course, we must be careful to exclude instances due to ophthalmia neonatorum from the category of antenatal cases.

Enlargement of the cornea (*macrocornea*) occurs in association with hydrophthalmus, and abnormal smallness (*microcornea*) in microphthalmus and also as the sole anomaly. *Conical* (dome-shaped) cornea may be an antenatal malformation (Gescheidt, *Ztschr. f. d. Ophth.*, ii. 483, 1832; A. Dujardin, *Journ. d. sc. méd. de Lille*, ii. 629, 1880; S. L. Frank, *Maryland Med. Journ.*, x. 273, 1883–84; O. Pincus, *Diss. inaug.*, Königsberg, 1887; and Steinheim, *Centrlbl. f. prakt. Augenh.*, xxi. 353, 1897); J. Tweedy (*Trans. Ophth. Soc. Unit. Kingdom*, xii. 67, 1891–92) is even of the opinion that the cases which appear in adult life are due to some predisposing embryological defect. *Dermoid tumours* of the cornea may be met with alone or in association with other ocular defects, such as coloboma of the lids; long hairs may grow from them in later life.

Malformations of the Iris.

Colour anomalies of the iris are not uncommon; they are rarely in existence in antenatal life, although the predisposition to develop them may be. At birth the colour is in all infants a greyish blue (due to the thinness of the iris tissue and the absence of pigment from its mesoblastic part), and anomalies in pigmentation come into existence later. The two irides may be of different colours (heterochromia): a mulatto with one brown and one blue eye was described by Bruns (*New Orleans Med. and Surg. Journ.*, n.s., xvi. 110, 1888–89), and the subject has also been dealt with by W. G. Sym (*Ophth. Rev.*, viii. 202, 1889) and J. Forrester (*Med. Rec.*, xlii. 399, 1892). An abnormal extension forward of the uveal pigment may cause dark nodules at the pupillary margin of the iris; this is "ectropion of the uveal pigment" (B. Wicherkiewicz, *Arch. f. Ophth.*, xxxvii. 1 Abth., 204, 1891). In albinism, that curious state which is sometimes hereditary and often shows family prevalence, the general absence of pigment is associated with local absence of it in the iris; the eyes of albinos, therefore, appear pink. It has been noted in twins (J. N. Hyde, *Internat. Med. Mag.*, i. 501, 1892), and among negroes (P. Topinard, *Assoc. franç. pour l'avance d. sc., compt. rend.* 1878, Paris, vii. 850, 1879; Smester, *Rev. d'anthrop.*, 2 s., ii. 675 1879; etc.). The albino eye has been specially studied by Broca (*Bull. Soc. d'anthrop. de Paris*, v. 141, 1864), by W. Manz (*Arch. f. Ophth.*, xxiv. 139, 1878), and G. M. Gould (Philadelphia, 1894); the iris tissue is of a grey colour, and the pink appearance is due to the interior of the eye seen through it.

The pupil may be slightly or markedly eccentric in position (*corectopia*); it may be associated with ectopia of the lens; cases are reported by A. Jaczynski (*Diss. inaug.*, Griefswald, 1889), Badal (*Bull. Soc. d'anat. et physiol. de Bordeaux*, xii. 253, 1891), W. M. Beaumont (*Trans. Ophth. Soc. Unit. Kingdom*, xiii. 146, 1892–93), A. Antonelli (*Atti di XI Cong. med. internaz.*, vi. oftal., 73, 1895), and by J. Brixa (*Klin. Monatsbl. f. Augenh.*, xxxvi. 432, 1898). The pupil may be abnormally small (*microcoria*); this may be due to fœtal iritis and the formation of posterior synechiæ; or it may be an original malformation. Again, there may be more than one pupil or *polycoria*, an anomaly which may arise through subdivision of the normal pupil (*e.g.* by a band of the persistent pupillary membrane) or by the appearance of supernumerary openings in the iris especially near its periphery. Numerous instances have been reported, including those by H. Wilson (*Med. Times and Gaz.*, i. for 1860, 392), P. D. Keyser (*Med. and Surg. Reporter*, xliii. 30, 1880), W. F. Mittendorf (*Trans. Amer. Ophth. Soc.*, iii., pt. 5, 735, 1885), G. E. de Schweinitz (*ibid.*, vi. 59, 1891–93), Fouchard (*Arch. méd. d'Angers*, i. 631, 1897), and E. Wingenroth (*Centrlbl. f. prakt. Augenh.*, xxiii. 105, 1899). In Mittendorf's observation the defect was hereditary (father and daughter).

A greater or less degree of *persistence of the pupillary membrane* of antenatal life is a comparatively common malformation of the iris (about 1 per cent.); it is also, as so many of the eye anomalies are, a malformation arising not in embryonic but in late fœtal life. It usually takes the form of fibres and tags, rarely that of a membrane; the fibres may constitute loops, or each may float from the iris with one end free, or they may pass to the capsule of the lens or adhere to the posterior surface of the cornea (Van Duyse, *Arch. d'opht.*, Avril, 1902, *Extrait*). A large literature relating to persistence of the pupillary membrane has grown up since Haller's dissertation on the subject appeared in 1758 (*Med. Chir. and Anat. Cases*, London, p. 122, 1758); references to many of the articles are in the *Index Catalogue*, xi. 860, 1890. Some recent cases are those of F. R. Cross (*Clin. Sketches*, i. 104, 1895), of W. F. Norris (*Trans. Amer. Ophth. Soc.*, vii. 594, 1897), and of M. Linde (*Centrlbl. f. prakt. Augenh.*, xxi. 81, 1897). The persistent tags vary in colour (grey, black, brown).

Absence of the iris (*irideremia* or *aniridia*) is another frequently recorded ocular anomaly. Long lists of references are in the *Index Catalogue* (vol. vii. p. 108, 1886, and second series, vol. viii. p. 343, 1903). The absence may be complete, the blackness of the pupil extending where the coloured iris ought to be; it may also be partial, and nodules or crescentic pieces of iris may be recognised. This anomaly has been explained in various ways, as by absence of the anterior ciliary arteries, by absorption (along with the pupillary membrane) in fœtal life, and by arrested development (due, perhaps, to strong union of the lens to the cornea from fœtal choroiditis). It is often associated with other ocular defects (*e.g.* ectopia of the lens, cataract, coloboma), and may show family prevalence (Henzschel, *Ztschr. f. d. Ophth.*, i. 52, 1830–31; V. Caudron, *Rev. gén. d'opht.*, vi. 16, 1887). It may also be transmitted hereditarily (Galezowski, *Rec. d'ophth.*, 3 s., ii. 122, 1880; J. A. Andrews, *Ophth. Rec.*, n.s., vii. 546, 1898), and may be met with in the children of parents with coloboma of the iris (S. Theobald, *Trans. Amer. Ophth. Soc.*, v. 99, 1888–89; De Beck, *Arch. Ophth.*, xv. 8, 1886; xxiii. 264, 1894).

The pupil may be altered in shape by absence of a portion of the iris (*coloboma of the iris*). The defect is usually in the lower part of the iris, but may be in other situations. Like coloboma of the eyelid, it may show all the degrees, from a slight notch in the margin up to complete absence of a segment of the iris. It may be associated with other defects of the eye, as with coloboma of choroid, microphthalmus and aniridia (of the opposite eye), as in the case seen by me in 1895 (*vide* p. 409). Heredity has been noted in connection with it (M. Rosskothen, *Diss. inaug.*, Kiel, 1898; F. P. Maynard, *Indian*

Med. Gaz., xxxii. 456, 1897; J. F. Streatfeild, *Ophth. Hosp. Rep.*, London, i. 153, 1858). Its teratogenesis is rather obscure, as there is no embryonic fissure in the iris whose persistence might be supposed to give rise to it; probably it results from defective closure of the fissure in the choroid and ciliary body, although this hardly explains the cases in which the coloboma affects the upper part of the iris; it may also be due to partial adhesion or late separation of lens and cornea.

"*Figures on the iris*" are due to irregularities in pigmentation or structure. In the case described by A. Claus (*Flandre méd.*, i. 65, 1894), the figures were "10" in the left eye and "45" in the right. Doubtless these irregularities in the iris have given origin to the tales of infants with names (*e.g.* Napoleon) in their eyes, and to the curious story related on page 120 of this volume (*q.v.*).

Malformations of Choroid.

Part of the choroid, usually of an ovoid shape, may be absent, giving rise to the anomaly known as *coloboma of the choroid.* No trace of this defect may be visible from the outside, but by means of the ophthalmoscope the exposed sclerotic is evident as a pearly white patch. Its situation is usually in the line of the so-called choroidal fissure (*vide* pp. 54, 66); but in C. A. Veasey's case (*Arch. Ophth.*, xxiv. 202, 1895) there was a double coloboma with a wide area of intervening healthy choroidal tissue, an arrangement very difficult to explain on the theory that such defects are due to want of closure of the fissure. It may coexist with coloboma of the iris and ciliary body; it may extend to the sheath of the optic nerve (A. H. Benson, *Dublin Journ. Med. Sc.*, 3 s., lxxiii. 177, 1882); and it may affect the macula (S. M. Burnett, *Arch. Ophth.*, xi. 461, 1882; Van Duyse, *Ann. d'ocul.*, xcvi. 139, 1886; *ibid.*, xcviii. 108, 1887). Macular coloboma has been noted also in the cyclopic eye (Van Duyse, *Arch. d'ophth.*, Extrait, jan.-févr. 1899). It may be present in both eyes (J. Eichhoff, *Diss. inaug.*, Bonn, 1878), or there may be a coloboma in one eye and aniridia in both (A. de Montmeja, *Rev. phot. d. hôp. d. Paris*, iv. 48, 1872). The malformation has been ascribed with some probability to adhesion of the retina to the mesoblast (Fuchs). Hereditary transmission has been observed. In albinism the *pigment* of the choroid is *absent.* (For recent literature on choroidal coloboma, see *Index Catalogue*, 2 s., iii. p. 623, 1898.)

Malformations of the Retina.

A comparatively common anomaly of the retina is the presence of an additional artery in the form of a branch from the posterior ciliary (W. Lang and J. W. Barrett, *Ophth. Hosp. Rep.*, Lond., xii. 59, 1888); and various abnormal arrangements of the vessels on the disk may be met with (W. A. Frost, *Trans. Ophth. Soc. Unit. Kingdom*, vii. 175, 1887; ix. 142, 1889). Pigmentary defects are found in albinism and in retinitis pigmentosa (which is occasionally congenital).

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With regard to the optic nerve, the direction of the nerve head may be reversed, the outer or temporal pale portion becoming the inner or nasal part. Sometimes opaque nerve fibres are discovered in the retina (L. Monesi, *Ann. di ottal.*, xxv. 603, 1896); they constitute bright white areas spreading out from the upper or lower margins of the optic disk; the anomaly is an arrested development, being due to the retention of the medullary sheaths around some of the axis cylinders. It has been said above that retinitis pigmentosa may be congenital, and several cases have been reported (Bousseau, *Bull. Soc. anat. de Paris*, xlii. 740, 1867; G. C. Harlan, *Amer. Journ. Med. Sc.*, n.s., lxiv. 130, 1872; P. Lagleyze, *Rev. argent. de oftal. pract.* (Buenos Aires), i. 19, 1883–84); it may be added (as a matter of peculiar antenatal interest) that it is one of the malformations which have been attributed to consanguineous marriages (H. Derby, *Boston Med. and Surg. Journ.*, lxxii. 149, 1865; J. Oakley, *Prov. Med. Journ.*, viii. 329, 1889), and it may show family prevalence (W. J. Cant, *Ophth. Rev.*, v. 245, 1886; R. Ramboldi, *Ann. di ottal.*, xii. 268, 1883).

Malformations of the Lens.

Aphakia (absence of the crystalline lens) may be found in association with microphthalmus; but it is doubtful whether it occurs alone, the cases which have been recorded being probably instances of displacement, not of absence (F. L. Parker, *Trans. S. Car. Med. Assoc.*, xxxi. 123, 1881). The lens may be *unusually small*, or it may show an abnormal curvature (*lenticonus*) of either its anterior or (more often) posterior surface, a somewhat rare anomaly (C. R. Agnew, *Arch. Ophth. and Otol.*, iv. 382, 1874–75). A defect in the margin of the lens (*coloboma lentis*) may be met with, but is comparatively rare (Schiess-Gemuseus, *Klin. Monatsbl. f. Augenh.*, ix. 99, 1871); it is generally associated with other anomalies, such as coloboma of the iris and choroid; and it is probably due to an arrested development of the suspensory ligament (A. G. Heyl, *Rep. Internat. Ophth. Congr.*, v. 16, 1876).

Ectopia lentis or congenital displacement of the lens may be in an upward or in a horizontal direction, or backward (in microphthalmus). It is usually bilateral, but may be unilateral. It is rare, but a sufficient number of cases has been reported to enable some conclusions to be drawn; among these may be mentioned the records of F. W. T. Sippell (*Diss. inaug.*, Marburg, 1859), Wecker (*Bull. Soc. de chir. de Paris*, 2 s., iv. 42, 1864), Delacroix (*Bull. Soc. méd. de Reims*, viii. 63, 1869), F. Duval (*Thèse*, Paris, 1874), C. J. S. Jeaffreson (*Ophth. Hosp. Rep.*, London, vii. 186, 1871–73), F. E. D'Oench (*Diss. inaug.*, Wiesbaden, 1879), and J. B. Roberts (*Phila. Med. Times*, xi. 280, 1880–81). It may be hereditary, and has occurred in five successive generations (A. S. Morton, *Ophth. Hosp. Rep.*, ix. 435, 1876–79); it may affect several members of the same generation (family prevalence), as in B. E. Fryer's record, where two sisters had double and symmetrical ectopia lentis (*Amer. Journ. Ophth.*, i. 54, 1884–85). The displaced lens may be small in size, and it may (rarely) show opacities in it; it may be associated with coloboma and also with aniridia and corectopia. It is probably caused by defective development of the suspensory ligament.

Congenital cataracts constitute an interesting group of lenticular anomalies. The opacity may be complete, when it varies in consistency (fluid, gelatinous, dense), and it is then probably due to persistence and thickening of the fibro-vascular sheath of the lens and of the central artery of the vitreous humour. The cataract, on the other hand, may be partial. It may then consist of small scattered opacities (streaks or spots) near the periphery, giving rise to "dotted" cataract; or it may be localised in the anterior pole of the lens (anterior polar or pyramidal cataract), a form which is to be distinguished from persistence of the pupillary membrane. It is doubtful whether a posterior polar cataract can be distinguished from persistence of the fibro-vascular sheath of the lens in that position. Again, zonular (lamellar) and nuclear cataracts of an antenatal nature are met with. A fairly large number of observations of congenital cataract (of various types) has now been accumulated; over one hundred and twenty references are given in the *Index Catalogue* (vol. ii. p. 752, 1881; 2 s., iii. p. 232, 1898). Heredity and family prevalence have both been noted over and over again in connection with the malformation, *e.g.* in the cases of Hübsch (*Gaz. méd. d'Orient*, x. 146, 1866–67), H. W. Williams (*Boston Med. and Surg. Journ.*, lix. 149, 1858–59), Baudon (*Rec. d'ophth.*, v. 9, 1878), A. D. Williams (*St. Louis Med. and Surg. Journ.*, xxxviii. 368, 1880), G. F. A. Appenzeller (*Diss. inaug.*, Tübingen, 1884), H. Wilson (*J. Ophth. Otol. and Laryngol.*, iii. 291, 1891), D. Webster (*Arch. Pediat.*, xi. 905, 1894), H. F. Hansell (*Ophth. Rec.* (Nashville), v. 488, 1895–96), Purtscher (*Centrlbl. f. prakt. Augenh.*, xxi. 198, 1897), and of many others. In many of the recorded cases successful operations for the antenatal blindness, resulting from the lenticular anomaly, were carried out.

Malformations of the Vitreous.

Almost the only important malformation of the vitreous humour is that due to persistence of the artery (central, hyaloid) which is present in early antenatal life, and normally disappears completely before birth. The hyaloid artery in its course through the vitreous is surrounded in one part of its extent by a hyaline membrane and in another by a cellular sheath, and various anomalies are produced by the persistence of the whole or of different parts of it and of its sheath. When the whole artery persists, the blood passing through it probably escapes by vessels in the posterior fibro-vascular sheath of the lens and ciliary body (Van Duyse, *Arch. d'opht.*, Mai, 1902, *Extrait*); but it may also persist but carry no blood, and it then stretches as a band from the optic disk to the posterior pole of the crystalline lens, or may end freely in the vitreous being attached either by its neural or lenticular extremity. The commonest form is that in which the neural end alone remains as a thin narrow cord lashing freely backwards and forwards in the vitreous humour. It may be that only a remnant of the hyaloid canal (canal of Cloquet or Stilling) persists, the artery itself having entirely disappeared (H. Schindelka, *Wien. med. Bl.*, vii. 358, 1884; H. Wilbrand, *Jahrb. d. Hamb. Staatskrankenanst.*, i. pt. 2, 430, 1890; L. Thilliez, *Journ. d. sc. méd. de Lille*, i. 289, 1897). References to about forty articles dealing with persistence of the hyaloid artery are given in the *Index Catalogue*, vols. i. 609, 1880; iv. 461, 1883; 2 s., i. 699, 1896; v. 249, 1900. This anomaly may be associated with other ocular malformations, such as coloboma of the choroid (Mitvalsky, *Arch. Ophth.*, xxiv. 192, 1895).

Malformations of the Nose.

Some of the malformations of the nose have been already described, such as mesial fissure (p. 378) and absence of the organ, or conversion of it into a proboscis, in cyclopia (p. 397); but some other anomalies require to be noticed briefly.

Slight deviations from the normal shape and size of the nose are common, so common as hardly to be accounted teratological. The organ may, for instance, be too *small* at birth, or, very rarely, too large and too *long*; these peculiarities also may show family prevalence and heredity. The so-called "*camois nose*" includes both the flattened nose (in which the nasal bones and ascending processes of the maxillæ may be absent and the septum very defective) and the snub or turned-up nose ("*nez retroussé*"); it, likewise, may be markedly hereditary. Paraffin has, of late years, been much used to try to correct such deformities. The twisted or *obliquely directed* nose is generally due to a deviation of the whole septum or of the anterior (cartilaginous) part of it; it is generally directed to the right side, and is accompanied by narrowing of the right nostril and nasal fossæ. Sometimes there may be a sort of scoliosis of the nose, the bones being directed to one side and the tip to the other. The palate may show an increased degree of arching and some unilateral irregularity; and there seems to be no doubt that in some instances, at least, the deviation of the nasal septum is truly antenatal, and that it is commoner in civilised than in primitive peoples. In the lower animals obliquity of the nose is a more extensive anomaly, being (in foals, pigs, and puppies) accompanied by deviation of the nasal, intermaxillary, and maxillary bones (*campylorrhinus*, Gurlt); the crossed beaks of birds are of a different nature (*e.g.* in the curvirostral passeres). Inclination of the cartilaginous septum alone to one side is a common nasal anomaly, and is associated with and perhaps caused by hypertrophy of the mucosa covering the inferior turbinated bone; but there is no reason to ascribe it constantly or even frequently to antenatal conditions.

The whole septum (both osseous and cartilaginous) may be absent in cases of cleft palate and defective premaxilla. In rare cases it may show in its anterior part a more or less circular perforation, which would appear to be occasionally antenatal in origin. About such congenital perforations, A. Rupp (*Med. Rec.*, xlvi. 771, 1894) states that they may either be due to perverse or arrested development (Germs' case) or to a pathological process implanted on the developing tissues (Klebs). It is possible that the custom among some savage races of perforating the nasal septum may have arisen from the birth of an infant with such an antenatal defect. In the septum above and in front of the recessus nasopalatinus may be found more or less marked traces (blind pouch, etc.) of the organ of Jacobson (A. Kölliker in F. von Rinecker's *Festschrift*, 1, 1877; G. Romiti, *Boll. d. Soc. tra i cult. d. sc. med. in Siena*, ii. 169, 1884; E. Schmidt, *Diss. inaug.*, Berlin, 1896; M. Mangakis, *Anat. Anz.*, xxi. 106, 1902).

Another antenatal malformation of the nose is the stenosis or atresia of the nares, anterior or posterior, unilateral or bilateral. The anterior nares may be narrowed or completely closed by membranous, cartilaginous, or even by osseous tissue on one or both sides (W. C. Jarvis, *Trans. Amer. Laryngol. Assoc.*, ix. 222, 1888). Congenital occlusions of the posterior nares or choanæ would seem to be less rare. The occlusion may be osseous, as in the cases of H. Luschka (*Arch. f. path. Anat.*, xviii. 168, 1860), Santesson (*Förh. v. Svens. Läk. Sällsk. Sammank.*, Stockholm, 303, 1866), Schrötter (*Monatschr. f. Ohrenh.*, xix. 97, 1885), and A. B. Thrasher (*Med. News*, lxvii. 79, 1895); and the bony anomaly may affect only one side, as in the cases of Sommer (*Wien. med. Presse*, xxiv. 476, 1883) and E. Zaufal (*Prag. med. Wchnschr.*, i. 837, 1876). The occlusion may be membranous, as in Ronaldson's interesting observation (*Trans. Edinb. Obstet. Soc.*, vi. 48, 1881). Stenosis or atresia at some point between the anterior and posterior nares has also been recorded; thus, there may be an adhesion between the middle or inferior turbinated bone and the septum (Bryant, *Lancet*, ii. for 1861, p. 207).

Median fissure of the nose has been already described, and I have also referred to lateral nasal fissures in the paragraphs devoted to hare-lip and oblique facial fissures. A median *dermoid cyst* of the nose is now and again met with, associated generally with a *fistula* lower down. In November 1900 I saw a case which was probably of this nature: the child was five months old, and had a small lump on the bridge of the nose, with a little opening lower down near the tip, from which some clear fluid occasionally escaped; the morbid state was congenital. The little patient was under Dr. M'Bride's care for suppuration from one ear. W. Lawrence (*London Med. Gaz.*, n.s., i. 472, 1837–38), Bramann (*Berlin. klin. Wchnschr.*, xxv. 1052, 1888), and others have published somewhat similar cases.

I bring this long chapter to an end with a reference to a malformation for which it is difficult to find a place in any system of classification. In April 1904 Dr. John Thomson kindly asked me to examine a female child, seven years of age, then under his care in the Sick Children's Hospital, Edinburgh. She was born with teeth, and her intelligence was below the average for her age; but the most striking peculiarity about her was the wide space between her two eyes and the thickening of the tissues of the nose. There was also a small coloboma of one eyelid on the left side, and the mouth was unusually wide and depressed at the corners. It seemed to me that this little girl possibly showed a minor degree of the newly established type *rhinodyme* (*vide* p. 233), in which there are two superior maxillæ and two noses, but these are so fused together as to constitute little more than an unusually wide face. The condition is the converse of cebocephalus.

CHAPTER XXIII

Merosomatous Terata (*cont.*): Malformations of the Lower Jaw and Ear; Nomenclature and Classification; Micrognathus; Agnathus; Cyclotia; Aprosopus; Absence of External Ear; Preauricular Appendages; Fistula Auris Congenita; Minor Malformations of the Pinna and of its various Parts (Helix, Anti-helix, Tragus, etc.); Distomus and Accessory Maxillæ.

THE malformations of the ear and lower jaw fall to be described in this chapter. From the ontogenetic point of view they are to be thought of as the anomalies associated with the first branchial arch and cleft; they are due to imperfect development or irregular rearrangement of the structures composing these transitory structures. Many of them obviously are arrested embryological processes.

Nomenclature and Classification.

The nomenclature and classification of the monstrous developments of the first branchial arch are in a chaotic state. Etienne Geoffroy Saint-Hilaire (*Philos. anat.*, ii. 97, 1822) saw a case of shortness of the lower jaw with conjunction of the ears, with deformity of the palate bones, and with fusion of the pterygoid processes of the sphenoid; this was in a sheep. Struck by the curious deformity of the sphenoid, Saint-Hilaire called the monstrosity *sphenocephalus*, and so initiated a series of terminological and classificational difficulties. Isidore Saint-Hilaire (*Histoire des anomalies*, ii. 420 *et seq.*, 1836) retained the name sphenocephalus for one genus of his family of *otocephalians*. The otocephalians, according to this author, are those in which the ears are approximated or united in the middle line, there is more or less marked atrophy of the lower part of the head, and the jaws and a great part of the face may be absent. They are subdivided into three groups, according as there are two distinct and separate eyes, a single eye or two united in one orbit, or no eyes at all. In the first of these three groups is the genus of the *sphenocephalians*, with the ears approximated or united under the head, and the jaw and mouth distinct. In the second are three genera—(1) the *otocephalians* proper, in which, in addition to the characters of the sphenocephalians, the eyes are fused (cyclops) and there is *no nasal proboscis*; (2) the *edocephalians*, in which there is a nasal proboscis above the single eye, the ears are approximated or united under the head, the maxillæ are atrophic, and there is no mouth; (3) the *opocephalians*, in which there is no proboscis, no mouth, atrophy of the maxillæ, a single eye, and approximation or fusion of the ears under the head. Finally, the third group (no eyes) contains the single genus of the *triocephalians,* in which the ears are again approximated or united under the head, the jaws are atrophic, there is no mouth or nasal proboscis, and the eyes are absent. As Taruffi (*Storia della teratologia,* vi. 389, 1891) has pointed out, this system of arrangement is defective: too much attention is paid to the state of the ears and too little to that of the lower jaw; the name *edocephalus* also is absurd, for although the nasal proboscis had been compared to the penis, there was no need to make use of such a comparison in framing a word. Gurlt (*Lehrb. d. path. Anat. d. Haus-Säugethiere,* ii. 110, 1832), meanwhile, being more impressed by the state of the jaw than of the ears, had constructed a place in his classificational system for *nanocephalus brachygnathus* (dwarf-head with short jaw), and had recorded an instance of it in a sheep. In 1877, Gurlt (*Ueber thierische Missgeburten,* 14, 1877) went a step further, and made a new species (*micrognathus*) to contain the cases in which there was apparent (not real) absence of the lower jaw, a small longitudinal fissure to represent a mouth, and approximation of the tympanic bones. The chief difference between brachygnathus and micrognathus was one of degree, the lower jaw being less developed in the latter than in the former. In *agnathus* the lower jaw is entirely absent.

Into this chaos of discordant classifications and names Taruffi (*op. cit.,* vi. 391, 1891) has tried to bring some order. He makes one group to include all the malformations showing defective development of the lower part of the face, and calls it *hypoprosopo-aplasia,* and subdivides this into *hypomicrognathus* (small lower jaw) and *hypoagnathus* (absence of lower jaw). He, also, has two separate groups: one for *cyclops* and *hypoagnathus* combined in the same specimen (fused eye and absence of lower jaw), and the other for the fœtuses whose faces have no eyes, no nose, and no mouth (*aprosopus*). Taruffi's and Saint-Hilaire's classifications cannot be entirely reconciled, for, while *hypomicrognathus* corresponds to *sphenocephalus, aprosopus* to *triocephalus,* and *cyclops hypoagnathus* to *opocephalus* and *edocephalus, hypoagnathus* and *otocephalus* are left unrelated. Recently, L. Blanc (*Journ. de l'anat. et physiol.,* xxxi. 187, 288, 1895) has expanded the Hilairean system into a still more complicated arrangement, has added three new types, and has endeavoured to show that the genus *otocephalus* of Hilaire's family of the otocephalians does not belong to that family at all, but is an intermediate type (*cyclotia*) between *otocephalus* and *cyclopia.* Blanc, like all modern teratologists, finds an embarrassment in intermediate types, very disturbing to attempts at exact taxonomy. I append Blanc's classificational system, which applies to the lower animals largely.

I. Transitional Types, including specimens of (1) defect of formation of the lower jaw (membranous state) without arrest of development of the first branchial arch, and (2) arrest of development of the first arch without other deformities than nasal and buccal occlusion.

II. Otocephalus—

Group 1. *Brain well formed.*

Type 1. *Ageniocephaly* — absence or rudimentary state of lower jaw, occlusion of isthmus of fauces, pharyngeal sac, approximation or fusion of middle ears, cranium and sense organs well formed, mouth exists.

Type 2. *Sphenocephaly*—absence or rudimentary state of lower jaw, occlusion of isthmus of fauces, pharyngeal sac, cranium and organs of vision well formed, mouth exists; but the superior maxillæ, squamous bones, and zygomatic arches are bent towards the middle line inferiorly, and the palate and pterygoid processes of the sphenoid and the tympanic cavities are approximated or fused in the middle line. Three subvarieties according to state of ears.

Type 3. *Agnathocephaly*—absence or rudimentary state of lower jaw, occlusion of isthmus of fauces, pharyngeal sac, cranium and brain well formed, eyes carried to lower surface of head, external ears approximated or united, no mouth, upper maxillæ folded and united by their alveolar border, zygomatic arches much approximated or fused, squamous bones, approximated or fused by their bases, tympanic cavities approximated or fused.

Type 4. *Strophocephaly* — absence or rudimentary state of lower jaw, occlusion of isthmus of fauces, pharyngeal sac, cranium and brain well formed, eyes displaced to lower part of face, external ears approximated or united, no mouth, superior maxillæ fused and atrophied, no zygomatic arch, one large orbit under anterior sphenoid, squamous bones united and fused under the posterior sphenoid, tympanic cavities approximated or fused.

Group 2. *Brain vesicular.*

Type 5. *Edocephaly*—absence or rudimentary state of lower jaw, occlusion of isthmus of fauces, pharyngeal sac, external ears approximated or united, no mouth, superior maxillæ fused and rudimentary, squamous bones fused under sphenoid, nasal proboscis present, eyes close together or fused under the anterior sphenoid, brain vesicular, no zygomatic arch, tympanic cavities approximated or fused, auditory ossicles deformed.

Type 6. *Opocephaly* — absence or rudimentary state of the lower jaw, occlusion of isthmus of fauces, pharyngeal sac, external ears approximated or fused, squamous bones fused under sphenoid, a single eye or one more or less double under anterior sphenoid, no proboscis, no bones of the face, very reduced frontal bone, vesicular brain, tympanic cavities approximated or fused, auditory ossicles deformed.

Type 7. *Spherocephaly*—absence or rudimentary state of lower jaw, occlusion of isthmus of fauces, pharyngeal sac, external ears approximated or united, no bones of face, no eye, no anterior sphenoid, squamous bones and frontal very reduced, brain vesicular, tympanic cavities approximated or fused, ossicles deformed.

Group 3. *No Brain.*

Type 8. *Triocephaly*—cranium reduced to the occipital, the petrous temporals (approximated or fused in middle line), and to a rudimentary parietal; no mouth, no eye, no nasal proboscis; external ears much approximated or united; brain reduced to medulla or pons and medulla.

III. TRANSITIONAL TYPE.—*Cyclotia* — shows combination of essential characters of both cyclopia and otocephaly.

I have given Blanc's arrangement in full in order that the reader may, by perusing it, gain some notion of the kind of malformations associated with defect of the first branchial arch, but it is too complicated as a scheme for use in human teratology, indeed some of the types described in it have not been recorded in the human fœtus, although, of course, they may yet be. I shall employ here the much simpler classification of Taruffi (*op. cit.*, vi. 388 *et seq.*, 1891), and shall discuss, in order, micrognathus (smallness of lower jaw), agnathus or hypoagnathus (absence of lower jaw), cyclops hypoagnathus (cyclops with absence of lower jaw), and aprosopus (absence of lower jaw and of several other parts of the face). Thereafter I shall take up some anomalies of the ear which hardly deserve the designation of monstrosities.

Micrognathus.

The leading character of this monstrosity is, as the name indicates, smallness of the lower jaw; there is a retreating chin of an exaggerated type, and a state of matters is produced which is the exact opposite of *cranium progenium* in which the chin projects. The deformity may be bilateral or unilateral; and it may be of medium degree (*leptomicrognathus* of Taruffi) when it is a simple shortness of the jaw, or of a high degree, when it is usually associated with actual defects in the jaw.

Lannelongue and Ménard (*Affections congénitales*, i. 423, 1891) have described an interesting series of cases of bilateral micrognathus. In one of these, a little girl two years old, the upper part of the face was normal in appearance, but below the mouth there was malformation. The lower lip lay on a plane posterior to the upper, and, the lower jaw failing to make the usual projection, the cheek passed directly into the neck. The mandible was both displaced backwards and atrophic, and there was a distance (antero-posteriorly) of about half an inch between the teeth of the upper and those of the lower jaw. The child was unable to separate the jaws, and even under chloroform the separation could not be carried out; so in all probability the glenoid cavity and the condyle of the jaw were malformed. The clinical result of the malformation was difficulty in feeding the child. In two other somewhat similar cases in much younger infants this difficulty was intensified by the coexistence of cleft palate, and resulted in death (in one case) at the age of twenty-three days; the tongue was small in size and was accommodated in the nasal fossæ. In yet another case there were other anomalies (double club-foot, muscular atrophy of lower limbs, scoliosis, and cicatrices of intrauterine adhesions over elbows and knees), pointing, perhaps, to an amniotic teratogenic cause. Sometimes the micrognathy is unilateral, and may then be erroneously regarded as an instance of congenital dislocation of the temporo-maxillary joint. E. Canton's case (*Trans. Path. Soc. Lond.*, xii. 237, 1860–61) was an instance of this: the left external ear was represented only by a fold of skin, the squamous temporal was flattened, zygomatic process was absent, the glenoid cavity showed a smooth surface and no cavity, and the left side of the lower jaw had no ramus and was only of the size that it ought to be at the age of two and a half years, although the individual was sixteen years old. I saw a child with a somewhat similar condition in November 1896; he was the sixth child of parents with eight children, none of whom were deformed save himself; the left side of the face was atrophic and the parts affected were the superior maxilla, the malar bone, and the mandible; the external ear of the same side was malformed and showed two fistulous openings, but there was no proper meatus. The patient was under the care of the late Dr. George Elder, and was No. 181 in my series of teratological records. Taruffi (*op. cit.*, vi. 393, 1891; viii. 538, 1894) has collected together sixteen observations similar in nature to the above, including a personal observation, and the cases of C. Adam (*Diss. inaug.*, Königsberg, 1887) in which the external ears and upper limbs were also deformed, of Maurice (*Ann. Soc. de méd. de St. Étienne et de la Loire*, i. 696, 1861), and of A. Marc (*Diss. inaug.*, Tübingen, 1892) in which the floor of the mouth was defective and the tongue was prolapsed under the chin.

Of the more advanced type of micrognathus Taruffi (*op. cit.*, vi. 395, 1891) collected together thirteen cases; to which may be added O. Bürger's observation (*Arch. f. Gynæk.*, lxviii. 295, 1903) in which, in addition to absence of the right half of the lower jaw (*hemignathus*) and right submaxillary gland, there was congenital amputation of the right arm at the wrist and of the left arm at the elbow. In A. Dugès' observation (*Rev. méd. franç. et étrang.*, iv. 407, 1827) it was the left half of the jaw that seemed to be absent. In two instances reported by Virchow (*Arch. f. path. Anat.*, xxx. 221, 1864) there were associated malformations (encephalocele, spina bifida, absence of radius, defective ears, preauricular appendages) along with a rudimentary condition of the mandible on one side. Not only is one side (or both sides) of the lower jaw small in size, but the condyle and sometimes also the coronoid process show deformities (B. Langenbeck, *Arch. f. klin. Chir.*, i. 451, 1861), as may the glenoid fossa and zygomatic process of the temporal bone (F. Trendelenburg, *Verletzungen und chirurgische Krankheiten des Gesichts*, 1886). Other instances of this malformation have been reported by A. Ogston (*Glasgow Med. Journ.*, 4 s., vi. 289, 1874), by S. Goldenstein (*Arrêt* *de développement de la machoire inférieure*, Paris, 1879), J. Wolff (*Berl. klin. Wchnschr.*, xxxiv. 256, 1897), and E. Kirmisson (*Compt. rend. Soc. d'obst., de gynéc., et de pædiat. de Paris*, iv. 153, 1902). Finally, it may be noted that the lower jaw may be more defective than in any of the cases described, may have neither angles nor alveolar borders, and may be fixed or "soldered" on to the superior maxilla; this was the state of matters in L. Calori's specimen (*Novi Comm. Instit. Bonon.*, ix. 29, 1849), which showed also no mouth, no uterus, no vagina, no anus, and had some digits wanting in the hands and feet.

Agnathus.

Agnathus is that monstrosity in which there is absence of the lower jaw. Taruffi prefers to call it *hypoagnathus*, to distinguish it from absence of the upper jaw, for which he reserves the name *epi-agnathus*, but the meaning of agnathus is quite well established and does not need this elaboration; further, the term epignathus is already in use for a type of parasitic twin, and is apt to be confused with Taruffi's epi-agnathus.

It is necessary here to refer to an extraordinary fact in Comparative Teratology for which no sufficient cause would appear to be forthcoming: I mean the great relative frequency of both micrognathus and agnathus among lambs. These monstrosities do also occur in puppies (Otto, *Lehrb. d. path. Anat.*, i. 184, 1814; I. G. Saint-Hilaire, *Histoire des anomalies*, i. 260, 1832), in pigs (P. Eckardt, *Diss. inaug.*, Breslau, 1889; B. Thompson Lowne, *Catalogue*, p. 70, 1893), in calves (G. Jäger, *Arch. f. Anat. u. Physiol.*, i. 64, 1826; iii. 74, 1828; Barrier, *Compt. rend. Soc. de biol.*, 6 s., iii. 271, 1877; E. F. Gurlt, *Ueber thierische Missgeburten*, p. 7, 1877), and in does (G. Jäger, *Arch. f. Anat. u. Physiol.*, i. 64, 1826; I. G. Saint-Hilaire, *Histoire des anomalies*, i. 259, 1832); but they are numerous, out of all proportion in lambs. Of micrognathus in the lamb we have records by G. Jäger (*loc. cit., supra*), by F. Eve (*Journ. Anat. and Physiol.*, xvii. 495, 1883) in a case in which it was unilateral, by E. L. Schubarth (*De maxillæ inferioris monstrosa parvitate et defectu*, 1819), and J. Reid (*Ann. Anat. and Physiol.*, i. 27, 1850); and of agnathus in the same animal there are the cases described by A. Dugès (*Rev. méd. franç. et étrang.*, iv. 436, 1827), by C. L. Barkow (*Nova Acta phys.-med. Acad. nat. curios.*, xv. 291, 1831), by A. G. Otto (*Monstrorum Sexcentorum Descriptio*, p. 334, 1841), by E. F. Gurlt (*Ueber thierische Missgeburten*, p. 6, 1877), who recorded as many as forty-five instances, by M. Duval et G. Hervé (*Compt. rend. Soc. de biol.*, 7 s., iv. 76, 1883), and by Thompson Lowne (*Catalogue*, p. 71, 1893). Why absence of the lower jaw should be so frequent in the lamb is not clear, but possibly it points to an undiscovered peculiarity in the ontogenesis of that animal; let comparative teratologists study this instance of predilection carefully, for it may contain some fact of illuminating power in this dark subject.

In the human subject agnathus is comparatively rare. I have not personally examined a specimen of it, save that in which it occurred along with cyclopia (Fig. 18); but Dr. Rogers some time ago sent me a photograph of a typical case, which I reproduce here (Fig. 66), and in September 1900 Dr. Elizabeth M'Elney sent me a photograph of a somewhat similar instance which had occurred in Birmingham. Rogers' case was published in 1898 (*Journ. Path. and Bacteriol.*, v. 137, 1898). The first reported instance seems to have been that of T. Kerckring (*Spicilegium Anatomicum*, obs. lx. p. 122, 1717); he states distinctly that the lower jaw was wanting in a five months' fœtus, and that the figure gives a better idea of the monstrosity than his description, but I am inclined to put it the other way, for the figure is sadly lacking in detail. Since Kerckring's case was published there have been about twenty further instances reported, including Underhill's specimen in which hydrocephalus coexisted (*Trans. Edinb. Obst. Soc.*, xi. 79, 1886), F. von Winckel's two fœtuses (*München. med. Wchnschr.*, xliii. 423, 1896), and S. A. Ewing's case (*Intercolon. Med. Journ. Australas.*, viii. 229, 1903).

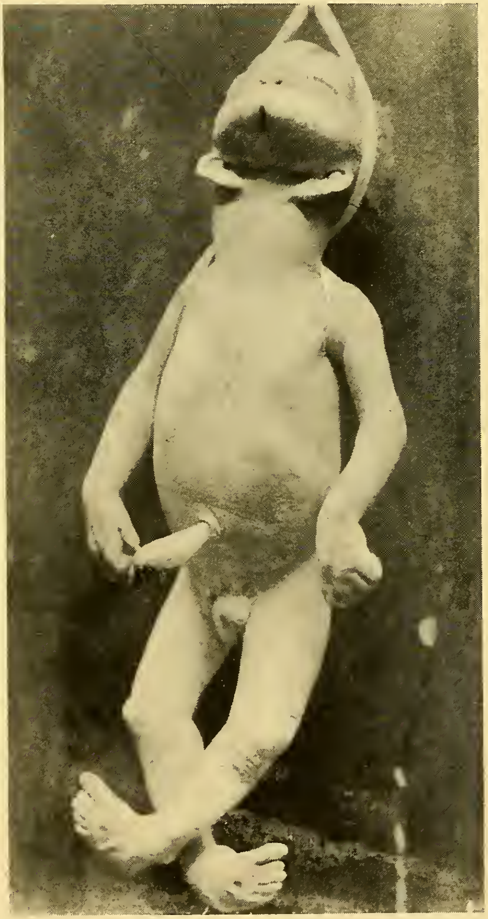
Fig. 66.—Dr. Rogers' Case of Hypoagnathus with Synotus.

The most striking feature of the monstrosity is the complete absence of a chin, the skin passing smoothly and continuously from just below the nose to the suprasternal region. There may be no external indication of a mouth (*astomus*), or there may be a small horizontal opening (*microstomus*), or a vertical slit (*hypostomus*), as in Rogers' specimen (Fig. 66). The external ears are displaced downwards and are approximated towards each other in the infranasal space where the chin ought to be. The degree of approximation of the external ears and of the deeper parts varies considerably: the pinnæ may be only slightly displaced downwards, there may be two auditory canals, and the two tympanic cavities may be united; or the two pinnæ may be furnished with a single median auditory canal, the tympanic cavities may be fused, and the malleus of one side may be joined to that of the other; or, again, there may be the same arrangement of external ears and tympanic cavities, with, in addition, the fusion of the squamous temporals by their zygomatic processes. Adolph Hannover (*Den menneskelige Hjerneskals Bygning ved Synotia*, Copenhagen, 1884) figures a typical specimen of the first of these sub-varieties of agnathus, or, as he terms it, *synotia*; in another well-reported case (Lannelongue et Ménard, *Affections congénitales*, i. 487, 1891) the tympanic bones were separated from each other only by an interval of half an inch.

The upper part of the face may be quite normal. Dissection reveals the fact that it is the first branchial arch and its associated structures whose evolution has been arrested. At first it may well be thought that the lower jaw is truly absent; but a careful search usually reveals a small fragment of bone in the middle line which represents the mandible, and behind which is a narrow pharyngeal sac communicating with the nasal fossæ and lying in front of the spinal column. F. von Winckel (*München. med. Wchnschr.*, xliii. 423, 1896) specially emphasises the presence of the mandibular rudiment in order to support his theory that the monstrosity is due to pressure (amniotic or other) acting upon the region of the first branchial arch and causing arrested growth, and not entire absence of the parts. The superior maxillæ are usually small likewise, the palate is narrow, and the body and wings of the sphenoid restricted. The buccal cavity is a cul-de-sac, having no connection with the pharynx, the soft parts which represent the floor of the mouth being united to the palate. There is usually a tongue, but it is often of small size, and may with the larynx lie at a lower level than usual, but the lowness of level is rather apparent than real. The hyoid bone may be present or it may be lacking; in the latter case the tongue also will be absent. Very marked defects are found in the temporal bones: they are displaced towards the lower part of the cranium and have no glenoid fossæ; they may not actually meet in this abnormal position, but in some cases they do unite so that the pinnæ and auditory canals are in contact or are fused into one (synotus); the tympanic cavities, also, may be conjoined or fused into one, and their ossicles (malleus, incus, and stapes) may be all present but in a deformed state. The posterior nares (choanæ) may be represented by a small opening or may be quite closed; in the former case they communicate with the pharyngeal sac. The pharyngeal sac, it may be added, sometimes communicates with the œsophagus.

Like all monstrosities, agnathus may occur in association with other malformations in the head or in more distant parts. Its combination with cyclopia is so important that it is described as a special type. Transposition of the viscera was noted in A. K. Hesselbach's case (cited by A. Förster, *Die Missbildungen des Menschen*, p. 95, 1865), and in those of A. W. Otto and Fæsebeck (cited by F. Ahlfeld, *Die Missbildungen des Menschen*, pp. 164, 166, 1882). In J. Arnold's specimen (*Arch. f. path. Anat.*, xxxviii. 145, 1867) there was a large cyst in the front of the neck communicating with the openings into the Eustachian tubes and larynx. In the case reported by S. Moos and H. Steinbrügge (*Ztschr. f. Ohrenh.*, x. 15, 1880–81) there were interesting anomalies of the internal as well as of the middle ears. The left suprarenal capsule was absent in Taruffi's specimen (*op. cit.*, viii. 402, 1894).

Both micrognathus and agnathus are most obviously of the nature of arrested developments of the first branchial arch. Doubtless when all the details of the complicated piece of organogenesis which results in the formation of the lower jaw are understood we shall know exactly why the characters of agnathus and synotus are just what they are; in the meantime there is in their teratogenesis much that is obscure. The careful dissection of specimens of the monstrosity may also throw light upon the embryology of the region. Dareste, it may be said, regarded otocephaly (including agnathus) as due to incomplete development of the medulla oblongata which allowed the auditory vesicles to come into close relationship with each other and to hinder the formation of the first branchial arches; but Blanc (*loc. cit.*) and others look upon the aural malformations as secondary and not primary, and see in arrested development of the first branchial arches the primary link in the chain of teratogenic events. The superior maxillary processes by their imperfect development or early union "bridle in," as it were, the lower part of the face and hinder its lateral growth.

Cyclotia (Cyclops Hypoagnathus).

Under the name of cyclops hypoagnathus, Taruffi (*op. cit.*, vi. 408, 1891) describes a type of monstrosity which combines in one the chief characters of cyclopia and of agnathus (with synotus). It is a more extensive malformation than either cyclopia or agnathus; and, from the embryological standpoint, it may be regarded as representing aplasia both of the nasal processes (with fusion of the parts normally separated by these) and of the first pair of branchial arches (with approximation or fusion of the structures between which they are interposed). It is a very monstrous type of monstrosity, the single eye and the displacement of the ears and the absence of the lower jaw combining to render the facial region most repulsive. This repulsiveness is well exhibited in the only specimen of this kind which I have had an opportunity of examining (Fig. 18).

It may be regarded as corresponding to the two genera of Saint-Hilaire, named *edocephalus* and *opocephalus*, and L. Blanc's group of monstrosities to which he gives the name *cyclotia*, to denote the composite nature of the teratological state. The outstanding features are the presence of a single or a double eye in the same orbital cavity, the union or approximation under the head of the two ears, and the more or less complete absence of the lower jaw; but there are others to which I must refer briefly. For instance, there may be a nasal proboscis lying above the single eye: this characterises the type named edocephalus by Saint-Hilaire and cyclops astomus rhynchænus by Gurlt; a good specimen of this is in my possession (Fig. 18). Sometimes, however, the nasal proboscis is quite rudimentary, as in the interesting case reported and figured by Lannelongue and Ménard (*Affections congénitales*, i. 492, 1891). A most extraordinary arrangement was met by H. Vogt in a specimen of which he was kind enough to send me a full account and which was afterwards published (*Norsk. Mag. f. Lægevidensk.*, 4 R., x. 639, 1895) under the name of "cyclops dirrhinus hypoagnathus"; it was a male fœtus, the product of a pregnancy complicated by hydramnios; the anterior fontanelle was almost closed; the two eyes were situated in a single orbit and had imperfect eyelids, and both *above and below* the orbit was a nasal proboscis, each provided with a small opening; there was no lower jaw or mouth, the ears were situated horizontally in the neck, and the external auditory meatus was represented by a small depression. Vogt's case would appear to be unique in the fact that it possessed two nasal projections, a supraorbital and a suborbital (Taruffi, *op. cit.*, viii. 540, 1894). Instances in which the nasal proboscis is wanting have been recorded by G. A. E. T. Knape (*Diss. inaug.*, Berlin, 1823), by C. Poelmann (*Ann. Soc. de méd. de Gand*, xxv. 229, 1850), by Christian Lovén (*Anatomisk beskrifning af ett cyklopiskt missfoster med defekt af ansigtets*, Stockholm, 1864), by C. Taruffi (*op. cit.*, vi. 414, 1891), and by M. H. Fussell (*Univ. Med. Mag.*, x. 337, 1898). The absence of the proboscis was used by Saint-Hilaire as the distinguishing feature of his genus *opocephalus*, and Gurlt emphasised it in his nomenclature, calling this type of monstrosity cyclops astomus arrhyncus.

There is usually no buccal opening or only a small aperture, but in Fussell's specimen (*loc. cit.*) there was a large mouth furnished with lips. Careful dissection will often reveal that the mandible is not really absent, but is represented by an osseous rudiment (E. Romey, *Diss. inaug.*, Königsberg i. Pr., 1892); this fact, it will be remembered, was noted and emphasised by Winckel in connection with agnathus (*loc. cit.*); in two of Thompson Lowne's cases (*Catalogue*, Nos. 261, 263, p. 75, 1893), however, there was apparently no trace of a lower jaw. In Koogler's specimen (*Amer. Journ. Med. Sc.*, n.s., lxxxiv. 129, 1882), dissected by R. M. Smith and A. J. Parker (*ibid.*, p. 132), the processus gracilis of each malleus turned inwards towards the median line and was united by a slender splint-like bone with its fellow of the opposite side; and this splint-like bone probably represented an undeveloped lower jaw.

The ears are approximated or fused and often show more marked deformities than in simple agnathus. There may be two auditory foramina (Lannelongue and Ménard, *loc. cit.*); and the tympanic rings may be united in the median line by an osseous arch, forming, as Lannelongue says, a small *pince-nez*; the cavity of the middle ear usually communicates directly with the pharyngeal sac (no Eustachian tube); and the tympanic ossicles are commonly present but in a malformed state. In some cases the ears may be so defective as to consist solely of a single auditory meatus opening directly into the pharynx (Knape, *op. cit.*); and the external ears may even be entirely wanting (Poelmann, *loc. cit.*).

The brain may show numerous anomalies. There may be no anterior separation into two hemispheres; fissures and convolutions may be almost absent (in Koogler's case the only fissure was that of Sylvius); and the corpus callosum, fornix, fifth ventricle, and septum lucidum may all be wanting. There may be coexistent hydrocephalus (R. Allan, *Lancet*, i. for 1848, p. 227); the cranium may be greatly deformed, exhibiting the state known as trigonocephalus (S. Sebenico, cited by Taruffi, *op. cit.*, vi. 411, 1891; M. H. Fussell, *loc. cit.*), or even anencephalus (von Lenhossék, *N. Jahrb. d. teutsch. Med. u. Chir.*, Bonn, iii. 1, 1821; W. Vrolik, *Tabulæ ad illustrandam embryogenesin*, Pl. xxvi., 1849). In Vrolik's case there was the further associated malformation of exomphalos.

Whatever may be found to be the causes of cyclopia and agnathus, they will also, it must be supposed, be active in cyclotia. L. Blanc (*loc. cit.*) further states his belief that cyclotia is a malformation lying midway between cyclopia and otocephalus (agnathus), and that there will yet be discovered a series of types of it running parallel with the different varieties of cyclopia and otocephaly; from the study of the specimens at present known it is quite likely that this conclusion will be established. Blanc also gives interesting details of this monstrosity as it occurs in the lower animals (lamb, pig, puppy, calf, kitten), and Taruffi (*op. cit.*, vi. 416, 1891) adds several interesting references.

Aprosopus.

Nearly all groups of types of terata have a sort of ultimate member in which the lowest grade of development along that special line is reached. In this and in the preceding four chapters I have been considering the monstrosities of the cranial and facial regions; in some of them the cranium is more or less defective, and in others the face; but I have now to consider a type in which both cranium and face are defective to the last degree. I modify this statement to the extent of saying *to the last degree possible in the fœtus that is not a twin* or a parasite upon another fœtus, for we shall find that in the allantoido-angiopagous twin (paracephalic, acephalic) a still lower grade of organisation of the head may be reached, when almost every trace of it is absent. To this very low form of cephalic organisation the name of *aprosopus* (α, πρόσωπον, without a face) was given by A. Dugès (*Rev. méd. franç. et étrang.*, iv. 407, 1827) in 1827; but the type itself was known in animals in the preceding century, and Etienne Geoffroy Saint-Hilaire had termed it *triencephalus* to indicate the absence of three parts, the mouth, the nose, and the eyes (*Philos. Anat.*, ii. 97, 1822). It cannot, however, be claimed that triencephalus of itself suggests any such meaning; and Isidore Saint-Hilaire's word *triocephalus* does not etymologically mark any great advance. L. Blanc (*Journ. de l'anat. et physiol.*, xxxi. 296, 1895) retains Saint-Hilaire's name triocephalus and invents a new name (*spherocephalus*) for some allied forms which differ, however, in the possession of a rudimentary brain. In a certain sense the group of aprosopous fœtuses as recognised by Taruffi (*op. cit.*, vi. 419, 1891) includes the triocephalic and most of the spherocephalic monstrosities (namely, those without a nasal proboscis and even a rudimentary eye). Another name which is synonymous is Gurlt's perocephalus aprosopus; but it is incorrect to place the cases of facial fissures, even when the fissures are many and deep, among the aprosopous fœtuses, for in the latter there is a continuous covering of skin in the region of the face, while in the former, of course, there is not.

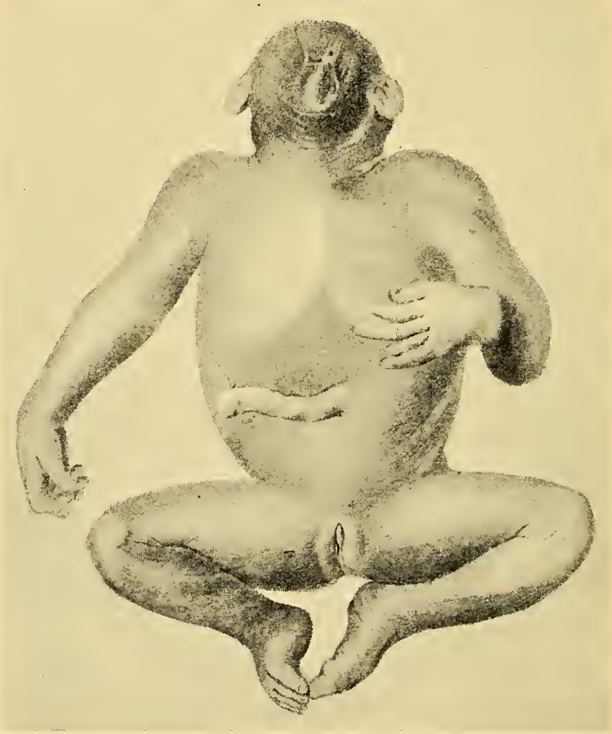

Fig. 67.—Case of Aprosopus, with Deformity of Left Hand. Specimen No. 19.

The aprosopous fœtus, then, may be defined as one possessed of a face, without nose, eyes, or mouth, but with a continuous covering of skin. It is a rare monstrosity in the human subject; Taruffi (*op. cit.*, vi. 421, 1891) has only succeeded in gathering together seven reported cases (including those of A. G. Otto, *Monstrorum Sexcentorum Descriptio*, No. lxxxviii. p. 54, 1841; of Vigla, *Arch. gén. d. méd.*, ii. 1849, p. 25; of G. Sapolini, *R. Ist. Lomb. d. sc. e lett. Rendic.*, Milano, 2 s., ii. 415, 1869; and of B. Thompson Lowne, *Catalogue*, No. 277, p. 78, 1893). In my collection of 326 cases I have met with only one instance of it (Fig. 67). It is more common in animals, Taruffi (*op. cit.*, vi. 433, 1891) having been able to collect 72 case-records of it—27 in lambs, 17 in puppies, 12 in pigs, 11 in kittens, and 5 in calves.

The aprosopous fœtus has a more or less globular head, something like the knob of a walking-stick; the skin covering it passes continuously into that of the neck. The only sense organs present are the external ears, which may be situated laterally, as in my specimen (Fig. 67), or may be approximated to each other in the middle line anteriorly (C. Pokorny's specimen, figured by Taruffi, *op. cit.*, vi. 423, 1891). There is usually some hair on the top of the head, and the circumference of the cranium sometimes does not greatly exceed that of the neck. Practically all the bones of the face are absent, save perhaps a trace of the lower jaw; the cranial bones, however, may be present and are usually firmly fixed together by osseous union, but sometimes the ethmoid and frontal bones may be wanting. The temporals are turned downwards and inwards, concealing the sphenoid; the glenoid cavities and zygomatic processes are absent; and the tympanic cavities are fused into one, the ossicles being also united together and fixed to the tympanic membrane. The petrous temporals may be fused or not. There is a pharyngeal cavity which may be quite closed anteriorly or may communicate with the external auditory meatus, or with a sac of unknown nature occupying the anterior part of the neck. There is usually a larynx as well as an œsophagus, but the hyoid bone and tongue may be absent or rudimentary. In the cranial cavity nothing else is usually found than serous fluid and the medulla oblongata; but in some of the specimens in animals small parts of the brain have been discovered, and in Vigla's case (*loc. cit.*) there was a cerebrum without convolutions but with a central cavity communicating with the fourth ventricle. L. Blanc (*loc. cit.*) uses the presence of a brain in some cases as a means of dividing the spherocephalics from the triocephalics (which have no trace of a brain beyond the pons and medulla or the medulla alone). Only the cranial nerves arising from the medulla are commonly present. Such are the leading characters of this type of monstrosity as they have been ascertained by Taruffi (*op. cit.*, vi. 429, 1891); but it is not easy to say which are essential and which occasional, for the number of specimens in the human subject that has been reported is so small, and it is not always safe to draw conclusions from cases in the lower animals.

In its teratogenesis, aprosopus requires us to imagine a complete arrest of the first branchial arches on both sides, and not simply a defect of their mandibular or maxillary processes. According to Dareste (*Production artificielle des monstruosités*, p. 370, 1891) the closure of the anterior part of the medullary groove takes place very early; the anterior cerebral vesicle does not develop, and the middle and posterior vesicles either do not develop or remain in the primitive state of a tubular structure very much like the spinal cord; in this way the formation of the head is interfered with. Dareste's views are founded upon observations on the chick, and it is possible that the explanation may not hold good for the human subject, and that the facial defects are primary and not secondary to cerebral ones. It would be necessary to know exactly all the details of the normal ontogenesis of the cerebral vesicles and first branchial arches, and especially of Meckel's cartilages in order to elucidate this problem, and Blanc admits that this is most difficult to achieve.

Absence of External Ear.

The external ear consists of the pinna or auricle and the external auditory meatus. In the strict sense of the term complete absence of the pinna and an imperforate state of the meatus constitute a rare malformation, but I may here conveniently include instances in which the pinna is rudimentary although not entirely wanting. It is an interesting fact that in the very ancient Chaldean tablets of Nineveh, as I have elsewhere pointed out (*Teratologia*, i. 131, 1894), there is a wonderfully complete list of aural deformities with their alleged prophetic significations; indeed the diviners of Mesopotamia seem to have had a knowledge of most of the deformities of the ears, nose, jaws, and mouth. The records are silent, again, regarding absence of the ear till the sixteenth and seventeenth centuries, when a few cases were reported, including that of F. Lachmund (*Miscell. Acad. nat. curios.*, Dec. i., Ann. vi.–vii., p. 239, obs. 178, 1677); in the eighteenth and nineteenth centuries several instances, more particularly of *rudimentary* pinnæ, were described.

In 1895, H. J. Stiles showed at a meeting of the Medico-Chirurgical Society of Edinburgh (*Trans.*, xv. 54, 1896) an infant of six months, whose pinnæ were represented by nothing more than small unconvoluted reduplications of skin, apparently containing no cartilage. There was no trace of an external auditory meatus on either side; the right half of the face was smaller than the left; on the left cheek there were two preauricular appendages; and the lower jaw was also poorly developed, a common accompaniment of auricular anomalies. This case is fairly typical of this variety of malformation. A somewhat similar case was described by J. Toynbee (*Month. Journ. Med. Sc.*, vii. 738, 1846–47), three others were put on record by Allen Thomson (*ibid.*, pp. 420, 729), and one of M. Hoffmann's patients constituted yet another (*Internat. med.-phot. Monatschr.*, iii. 357, 1896).

What represents the external ear is usually little more than a fold of skin or a piece of cartilage in a cutaneous covering situated on the side of the head with its long axis vertical; sometimes, however, there are two or more tags of cartilage-containing skin irregularly placed and not always occupying the normal position of the ear. The deformity may be unilateral or bilateral: in one of Gradenigo's three cases it was bilateral (Taruffi, *op. cit.*, vi. 551, 1891). The meatus auditorius is usually obliterated: it may be represented by a slight fossa, or there may be no sign of it at all; the little openings sometimes seen anterior to the normal position of the ear, in these cases, do not necessarily indicate the meatus, for they may be fistulæ.

In a small number of cases, post-mortem examinations were carried out upon individuals with absence or rudimentary development of the pinna. In several of them a cartilaginous meatus was found, but it ended blindly, and the tympanic ring and membrane were represented simply by a small piece of bone. The tympanic cavity and the osseous part of the Eustachian tube may be found; but they are both small in size, and the auditory ossicles may be malformed or defective. The labyrinth, however, is usually normal, a fact which accounts for the degree of hearing possessed by some patients suffering from this malformation, and a circumstance which is embryologically explicable by the independence of the ontogenesis of the inner and middle ears.

Associated malformations are not uncommon. There may, for instance, be cleft palate (T. Heiman, *Ztschr. f. Ohrenh.*, xxi. 271, 1890–91), absence of nose, imperforate anus, and polydactyly (W. Duncan, *Trans. Obst. Soc. Lond.*, xxxvii. 16, 1895), hare-lip and cleft palate (W. Anton, *Prag. med. Wchnschr.*, xxii. 235, 249, 1897), absence of a thumb (F. S. Pluskal, *Oesterr. med. Wchnschr.*, p. 1373, 1844), enlargement of the buccal commissure (Le Briero, *Gaz. d. hôp.*, xxxiv. 122, 1861), or preauricular appendages (*q.v.*). The malar bone may be absent.

Attempts to improve the hearing powers by operative measures (cutting down in the position of the meatus, etc.) have not been successful, a fact which is largely to be accounted for by the defective state of the middle ear, and by the cicatricial constriction which follows (Lannelongue et Ménard, *Affections congénitales*, i. 522, 1891). For purely æsthetic purposes an artificial ear will probably be more satisfactory than any plastic operation.

The malformation (called *ecto-otus-aplasia* by Taruffi) is obviously to be explained as an arrested development of the first branchial cleft and adjacent structures. If, as Gradenigo maintains, the pinna is derived in part from the mandibular process of the first branchial arch and in part from the second branchial arch, then it is probable that the cartilaginous tags which are sometimes to be found may represent one or other of these two portions (mandibular and hyoidal). The cause of the arrested development may be pressure, *e.g.* amniotic.

I may add here some further bibliographical references: D. S. St. J. Roosa, *Trans. Amer. Otol. Soc.*, p. 123, 1873; Bidder, *St. Petersb. med. Ztschr.*, n.F., iv. 388, 1873–74; Chowne, *Lancet*, ii. for 1860, p. 59; H. Knapp, *Arch. Otol.*, x. 119, 1881; xxi. 438, 1892; E. R. Corson, *N. York Med. Times*, xiv. 50, 1886–87; E. Joel, *Ztschr. f. Ohrenh.*, xviii. 278, 1887–88; C. H. Vilas, *Trans. Amer. Homœop. Ophth. and Otol. Soc.*, vi. 29, 1882; A. Robertson, *Glasgow Med. Journ.*, xxxi. 209, 1889.

Preauricular Appendages.

Preauricular appendages may be *defined* as skin-covered projections, of varying number, size, and form, situated either immediately in front of the pinna or at some point in the line passing from the external ear to the angle of the mouth of the same side, and usually containing an axial nucleus of cartilage. I have examined two such cases (*Teratologia*, ii. 14, 1895): in one the appendage was single and was situated immediately in front of the left ear of a boy twelve years of age; in the other, there was a group of appendages lying in front of the ear and surrounding a small sinus, from which a little glairy fluid occasionally exuded. To cases like the latter the name supernumerary auricle (*polyotia*) has sometimes been given; but it is very doubtful whether they can in any sense be regarded as true additional ears (*e.g.* J. Birkett's case, *Trans. Path. Soc. Lond.*, ix. 448, 1857–58).

This malformation has long been known to occur, for in the Chaldean teratological lists, already several times referred to (*Teratologia*, i. 135, 1894), there is the record of an infant born "with two ears on the right side." The earliest cases reported in recent times seem to have been those of Saviard (*Nouv. Rec. d'observ. chir.*, obs. 116, p. 514, 1702), and other instances in the eighteenth century were those of Sue (*Hist. Acad. roy. d. sc.*, Ann. 1746, p. 42, 1751), of G. H. Fielitz (*Arch. f. d. Geburtsh.*, ii. 71, 1789), and of J. C. Stark (*N. Arch. f. d. Geburtsh.*, i. 415, 1798).

During the nineteenth century many observations were recorded, of which I have given elsewhere a fairly complete bibliography (*Teratologia*, ii. 34, 77, 1895) of over fifty references; specially valuable papers are those of Virchow (*Arch. f. path. Anat.*, xxx. 221, 1864), of J. H. Morgan (*Trans. Med.-Chir. Soc. Lond.*, lxv. 13, 1882; *Illustr. Med. News*, ii. 265, 1889; *Trans. Clin. Soc. Lond.*, xxix. 218, 1896), of Lannelongue (*Cystes congénitaux*, p. 171, 1886), of Majocchi (*Ateneo med. parmense*, Ann. i. 75, 1887), and of Bland-Sutton (*Illustr. Med. News*, i. 320, 1888; vi. 99, 1890).

Various *names*, more or less synonymous, have been given to these little appendages, such as "excrescences," "warts," "tubercles," "supernumerary auricles," "branchial fibro-chondromata," "preauricular papillary teratomata," "supernumerary tragus," and "accessory auricles." They are comparatively *frequent*, for among fifty thousand children examined by F. Warner (*Brit. Med. Journ.*, ii. for 1894, p. 197) there were thirty-three cases—twenty-one boys and twelve girls.

The *clinical history* is sometimes interesting. There was an alleged maternal impression in the cases of Moxhay (*Brit. Med. Journ.*, ii. for 1870, p. 521) and C. Apfelstedt (*Diss. inaug.*, Jena, p. 28, 1892). In J. L. Reverdin's observation (*Rev. méd. de la Suisse rom.*, vii. 458, 1887) there was family prevalence (three out of five children), and the father had a supernumerary nipple on his chest; and in one of J. J. H. Kratz' cases (*Diss. inaug.*, Bonn, 1880) a sister of the individual with preauricular appendages had a bilateral fistula auris congenita. Cranial and facial defects have been shown to be common in the relatives of the subjects of this aural malformation (Féré, *La Famille Nevropathique*, 214, 1894). The appendage itself does not interfere with the health of the bearer of it, except when there are other malformations, such as absence of the zygoma of the temporal bone in Walker Downie's patient (*Practitioner*, lvi. 261, 1896). In two female patients it became larger and more erectile during menstruation, and was regarded as an aberrant mammilla (A. Barth, *Arch. f. path. Anat.*, cxii. 569, 1888; P. Eyle, *Ueber Bildungsanomalien der Ohrmuschel*, p. 28, 1891). Hearing was occasionally defective, doubtless from associated malformations (Virchow, *loc. cit.*; J. H. Morgan, *loc. cit.*, 1882). These appendages occur with equal frequency in both sexes; they are always truly congenital; they grow slightly or not at all in postnatal life; and they can be removed easily and with impunity.

With regard to their *morbid anatomy*, they are more commonly unilateral than bilateral. In the records collected together by me (*Teratologia*, ii. 24, 1895) their number varied from one to four: in fifty cases there was a single appendage in front of the ear, in twenty there were two, in thirteen three, and in one four; and in two instances (Mignot, cited by Broca, *Bull. Acad. de méd.*, p. 1217, 1879; Apfelstedt, *op. cit.*) there was a group forming a structure resembling a whole pinna. Their size varied from that of a pinhead to that of a pea or bean; in one of my cases the appendage, cylindrical in shape, measured 1·3 cm. in length, and had a uniform circumference of 1·5 cm. Although commonly cylindrical, they are occasionally flat, conical, bifid, trifid, or with a bulbous free extremity. They are most often situated immediately in front of the tragus; frequently they lie in front of the crus helicis, less frequently on the crus itself; they may be found on the cheek itself in the line leading from the auricle to the angle of the mouth; and they have been seen, but rarely, on the lobule of the pinna. Their consistence is like that of the lobule of the ear, but a firmer central part can sometimes be palpated; and they commonly stand out from the surface of the face. In structure they may consist of no more than skin covering an axial rod of condensed connective tissue (as in one of my cases, Fig. 68); in other instances there is a core of reticular or of hyaline

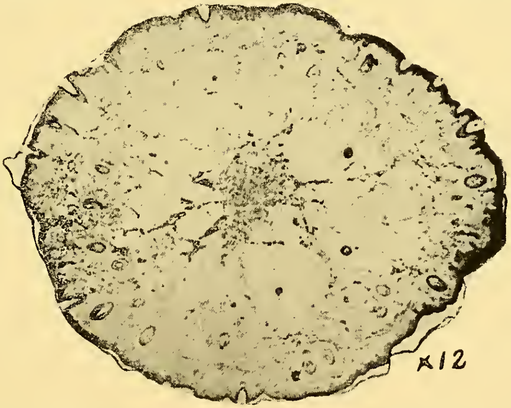

FIG. 68.—Transverse Section of Preauricular Appendage (Low Power).

cartilage, which may be inserted into the fascia lying between the temporal and masseter muscles. The skin has its usual microscopic characters, and sometimes there is a tuft of hairs at the apex of the appendage. There may be a marked adipose layer; but in my case (Fig. 69) there was no fatty stratum, but simply one of fine areolar tissue, such as is seen in the fœtus before the deposition of the fat.

Associated malformations are common and somewhat interesting. In some instances there are grave monstrosities; as in Meckel's specimen (*Arch. f. Anat. u. Physiol.*, p. 36, 1826), in which there was one umbilical artery, various deformities of the limbs, absence of one lung and of one kidney, and a communication between the rectum and bladder. Generally the ears are defective, and the defect may take various forms: there may be absence of the ear (R. Müller, *Diss. inaug.*, Kiel, 1893), or a congenital fistula (Hartmann, *Compt. rend. d. IV Congr. internat. d'otol.*, p. 15, Brussels, 1889), or occlusion of the meatus (Billard, *Traité d. mal. d. Enfans nouveau-nés*, 3rd edit., p. 53, 1835) or narrowness of it (Lesser, *Deutsche Ztschr. f. Chir.*, ii. 311, 1873), with bifidity of the tragus, etc. etc. There may also be defects in the deeper parts, such as malformations of the tympanic ossicles (M. Schultze, *Arch. f. path. Anat.*, xx. 378, 1861) or absence of them and of the tympanic ring and membrane (G. Mori, *Ann. univ. di med.*, ccxxxii. 250, 1875). Again, there may be associated ocular anomalies, such as microphthalmus, lengthening of palpebral fissure (R. Morian, *Arch. f. klin. Chir.*, xxxv. 286, 1887), and coloboma of an eyelid. The mouth also may be deformed: there may be cleft palate, or hare-lip, or a defective mandible, or absence of the temporo-maxillary

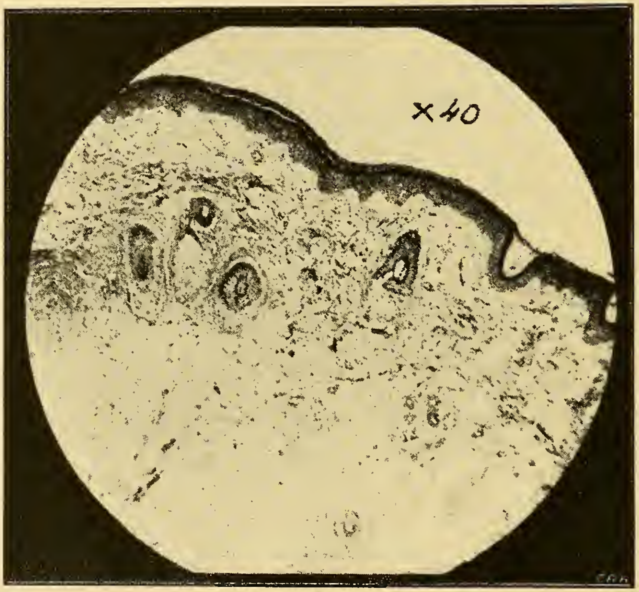

FIG. 69.—Microscopic Section of Preauricular Appendage (High Power).

joint, or lemurian apophyses of the jaw (Féré, *op. cit.*), or (most frequently) macrostoma (Sir W. Fergusson, *Lectures on the Progress of Anatomy*, p. 56, 1867; L. Reismann, *Arch. f. klin. Chir.*, xi. 858, 1869; Roulland, *Bull. Soc. anat. de Paris*, 4 s., xi. 599, 1886; L. Leplat, *Ann. Soc. med.-chir. d. Liège*, p. 647, 1888). The coexistence of congenital fistulæ has already been noted; and there may be cervical auricles (L. Bernacchi, *Atti Assoc. med. lomb.*, No. 1, p. 70, 1892).

In an article which I published in 1895 (*Teratologia*, ii. 65, 1895) I discussed with considerable fulness the views that have been held regarding the *teratogenesis* of preauricular appendages. I there referred in detail to the views of Schultze (*loc. cit.*), of Virchow (*loc. cit.*), of Sir James Paget (*Trans. Med. Chir. Soc. Lond.*, lxi. 46, 1878), of Van Duyse (*Ann. Soc. de méd. de Gand*, lx. 141, 1882), of J. H. Morgan (*loc. cit.*), of Bland-Sutton (*Evolution and Disease*, pp. 82–92, 1890), of Lannelongue and Ménard (*op. cit.*), and of Gradenigo (in Taruffi's *Storia*, vi. 566, 1891). The main ideas underlying these theories are that preauricular appendages are branchial in origin; that they are displaced projections which ought to have taken part in the formation of the external ear; that they represent, in atavistic fashion, the opercular skin-folds of animals lower down in the zoological scale; that they are inflammatory productions arising along the margins of the first branchial groove; or that they arise by budding from the margins of the cleft in the same ontogenetic way as the tubercles that form the ear arise. Gradenigo thinks, and his theory differs essentially from the others, that the preauricular appendage represents a persistence of the crus prætragicum helicis, of which normally there is no trace in the human subject, but which is well seen in some rodents; it is to be seen, however, at an early stage in embryonic life. Now, I think there can be no doubt that preauricular appendages represent an arrested or diverted or arrested and diverted state of the ontogenesis of the external ear region in the embryo. Some six tubercles or colliculi are grouped round the first branchial cleft, or hyo-mandibular fissure, to form by their fusion the pinna; but in addition to these there are other fissures and processes which abound in the peri- and pre-auricular region. Keeping in mind the nature of the associated malformations and the various positions occupied by the appendages, I do not think that they are invariably due to an abnormality in the closure of any one fissure or in the growth of any one process. When they occupy their usual position immediately in front of the tragus one naturally thinks of an anomaly in the evolution or involution of the posterior end of the hyo-mandibular (or first visceral) cleft, or of its adjoining mandibular and hyoidal arches; whilst when they occur further forwards on the cheek one suspects some abnormality in the development of one of the other facial processes and fissures, such as the intermaxillary.

I am inclined to regard the appendages themselves as due to a sort of budding from the margins of one or other of these fissures, or from the processes, or in some cases from the colliculi or helices themselves. In fact, the external ear is to be regarded as produced by a series of buds arising around the posterior end of the hyomandibular cleft, and it seems to me that the cause which normally produces the pinna may also, in abnormal conditions, lead to the formation of the appendages.

What, however, is the nature of this cause? There can, I think, be only one answer to this question: the primary factor is the amnion. Whether it is necessary to predicate also an abnormal state of the fissures and processes themselves is doubtful, but I am inclined to believe that the amnion may by an unnatural tightness or by an unusual agglutinativeness prevent the normal closure of the fissures, whilst it is also possible that the margins of the fissures may possess this same agglutinative character, which may be of an inflammatory nature. But I must refrain from entering again in detail into the general theory of amniotic action in teratogenesis, already discussed at length in Chapter XI. It may, however, be said in conclusion, that cervical auricles or appendages will probably be found to be explicable by the same teratogenetic theory as preauricular ones, for they are apparently of the same nature.

Fistula Auris Congenita.

Fistula auris congenita, which is generally preauricular in position, is a malformation of little importance; but it has, however, a slight interest on developmental grounds. It may easily be overlooked, for it has a very small opening, and this is often obscured by a small crust, formed by the drying of the slight secretion which exudes from it.

Fistulæ may occur in various situations on and near the ear, but, perhaps, the term *fistula auris congenita* ought to be reserved for that which lies at the point of junction of the crus helicis and the crus, or a little anterior to the crus and to the tragus; at any rate it is used in this work in that sense. Since it was first clearly described by Heusinger (*Arch. f. path. Anat.*, xxix. 361, 1864) and had its antenatal origin established, many instances have been reported. According to P. Eyle (*Diss. inaug.*, Zürich, 1891) and others, these fistulæ occur in about two per 1000 cases; but, on account of their strongly developed hereditary character, one observer may easily happen to have seen six, eight, or ten of them without having examined many thousand ears.

Their *clinical features* are comparatively unimportant: they cause almost no disfigurement, except in the cases in which they give rise to a retention cyst (through blocking of the fistulous tract). They secrete a small quantity of serous or milky fluid, which occasionally forms a scab over the orifice. They do not appear to be more common in one sex than in the other; but, as has been stated above, they are often peculiarly hereditary. In one of the case-records of J. J. H. Kratz (*Diss. inaug.*, Bonn, 1880) a mother and all her sons had this deformity; in V. Urbantschitsch's interesting article (*Monatschr. f. Ohrenh.*, xi. 85, 1877) there are instances of heredity in which the first born seemed specially to participate; and Paget (*Med.-Chir. Trans. Lond.*, lxi. 41, 1878) saw the deformity in seven members of the same family, and in some of these and in their relatives there were also fistulæ of the neck. Other instances were reported by D. Schwabach (*Ztschr. f. Ohrenh.*, viii. 103, 1879), F. P. Lewis (*Journ. Ophth. Otol. and Laryngol.*, iii. 14, 1891), and P. Eyle (*op. cit.*); in the latter the defect could easily be traced for four generations, it affected males and females, and it was bilateral in some individuals.

In its morbid anatomy the fistula is a small narrow tract from ·5 to 1 cm. in length, which is directed downwards and forwards from the crus helicis, and ends blindly, never, apparently, opening into the auditory meatus. It has a slightly raised margin. It seems to be as common on the right side as on the left, and it may be bilateral, although most commonly it is unilateral. I have only seen two cases of it (unilateral); but that is not surprising, for I have not specially looked for it, nor has my attention been specially focussed upon it. When the secretion is retained for any cause, a cyst may result, as in the cases reported by F. Schmitz (*Diss. inaug.*, Halle, 1873), C. J. Kipp (*Trans. Amer. Otol. Soc.*, ii. 402, 1875–81), V. Urbantschitsch (*loc. cit.*), Lannelongue and Ménard (*Affections congénitales*, i. 221, 1891); ulceration may also occur in the neighbourhood (C. Mettenheimer, *Memorabilien*, xxv. 100, 1880). Occasionally there is no true fistulous tract, but only a depression or fossa, with a cicatricial area of skin surrounding it; this, likewise, may be hereditary, as in one of Gradenigo's cases (in Taruffi's *Storia della teratologia*, vi. 573, 1891). *Associated malformations* are common in connection with fistula auris congenita. Among these reference may specially be made to preauricular appendages (Hartmann, *Compt. rend. d. IV Congr. internat. d'otol.*, p. 15, 1889; H. Knapp, *Trans. Amer. Otol. Soc.*, ii. 357, 1875–81; Roulland, *Bull. Soc. anat. de Par.*, 4 s., xi. 599, 1886); to anomalous states of the pinna, such as absence or rudimentary development (C. F. Heusinger, *Specimen malæ conformationis organorum auditus humani*, Jenæ, 1824; Toynbee, *loc. cit.*) or contortion (F. Rohrer, *Tagebl. d. Versamml. deutsch. Naturf. u. Aerzte*, lviii. 137, 1885); and to cervical fistulæ (Heusinger, *Arch. f. path. Anat.*, xxix. 361, 1864; Urbantschitsch, *loc. cit.*).

The hypothesis which has been generally accepted regarding the teratogenesis of fistula auris congenita is the persistence of part of the first branchial cleft; but it must be admitted that there are two difficulties (at least) in the way of a full and free acceptance of this view. The first is the freedom of the middle ear from participation in the deformity, and the other is the position of the fistulæ. Gradenigo (in Taruffi's *Storia*, vi. 580, 1891), from a study of the development of the crus helicis, comes to the conclusion that fistulæ result from insufficient closure of the sulcus between the crus pre- or supra-tragicum and the crus helicis, or between the crus supra-tragicum and the tragus; he does not think that the coexistence in some cases of fistulæ in the neck (due to branchial anomalies there) is of any higher value (in argument) than that of a coincidence. In the meantime the question whether fistula auris is due to delayed union of such a primary fissure as the first branchial or of such a secondary one as the sulcus between two parts of the external ear, must be left with a *non liquet.* It may be added, although the theoretical value of the statement be obscure, that fistulæ in this position would appear to be commoner in the lower animals than in man.

Other references on this subject (in addition to those already given) are as follows:—Pflüger, *Monatschr. f. Ohrenh.*, viii. 132, 1874; T. M. Girdlestone, *Austral. Med. Journ.*, n.s., i. 322, 1879; E. Dyer, *Trans. Amer. Otol. Soc.*, iii. 468, 1882–86; K. Bürkner, *Arch. f. Ohrenh.*, xxii. 200, 1885; R. T. Morris, *N. York Med. Month.*, i. 169, 1886–87; A. B. Randall, *Trans. Amer. Otol. Soc.*, iv. 485, 1887–90; A. Hahne, *Diss. inaug.*, Göttingen, 1889; J. Gruber, *Aerztl. Ber. d. k. k. allg. Krankenh. zu Wien*, 185, 1891; A. Schwendt, *Arch. f. Ohrenh.*, xxxii. 37, 1891; Peugniez, *Gaz. méd. de Picardie*, xi. 481, 1893; Vauthier, *Ann. de la Policlin. de Paris*, iii. 95, 1893; C. Grunert, *Arch. f. Ohrenh.*, xlv. 10, 1898.

Congenital fistulæ have been occasionally met with in other parts of the ear, and especially in the lobule (J. Sabrazès, *Bull. Soc. d'anat. et physiol. de Bordeaux*, xii. 124, 1891; Lannelongue and Ménard, *op. cit.*, p. 225; Betz, *Memorabilien*, viii. 135, 1863; Bland-Sutton, *Evolution and Disease*, p. 179, 1890). In Bland-Sutton's case the fistula was so complete that an earring was suspended in it a few days after birth. Of course such fistulæ have suggested the transmission of an acquired character (ear-boring); but it seems to me that the birth in very ancient times of an infant with this malformation may have suggested to a tribe, or to mankind generally, the practice of ear-boring. The traumatism may not have caused the congenital malformation, but, in a sense, the occasional occurrence of the malformation may have led to the frequent infliction of the traumatism!

Minor Malformations of the Pinna.

The chief importance of minor malformations of the external ear is in relation to what are called the stigmata of degeneration. "The external ear," writes E. S. Talbot (*Degeneracy*, p. 207, 1898), "is, of all organs, that most affected by degeneracy." I pointed out (in the first section of this MANUAL, p. 97, Fig. 14) that the ears are among the parts of the body which finish their embryology in the fœtal period of antenatal life; their morphological differentiation is not completed in the embryonic period, when that of most of the other parts of the body is, but is postponed till the later fœtal epoch. Malformations of the ears, therefore, although embryological in nature are fœtal in time. Now most of the stigmata of degeneracy agree with them in this comparatively late origin in antenatal life (*e.g.* the jaws, teeth, skin, eyes, hands, feet, etc.), and, further, it is about this time also that many minor cerebral defects arise. If we imagine some common morbid cause (toxic, toxinic, microbic) coming to act upon the organism during this epoch it is easy to understand how mental defects, aberrations of the nervous system, and minor physical defects of ear, skin, eye, and digits are all found associated together. Statistics show that in the criminal and in the insane, the minor malformations of the external ear are more common than in individuals of normal mental and social qualities.

These minor malformations may now be briefly indicated. There may be asymmetry of the pinnæ, one of them being inserted higher or lower or more to the front than the other, or one being larger than the other. Marked displacements, *e.g.* downwards and forwards into the neck, are usually associated with other grave defects (*e.g.* agnathus); but slight displacements may occur, either alone or in combination with macrostoma, etc. The ears may be more bound down to the head than usual; and the so-called "jug-handled" (or Morel) ear is a long and narrow organ attached in its entire length, including the lobule. On the other hand, the pinna may stand out from the side of the head in a prominent fashion ("orecchio ad ansa," *Lombroso*) and to a varying degree; with this there may be a folding of the pinna upon itself; so marked may be the deformity that plastic operative interference may be attempted for its relief (E. T. Ely, *Arch. Otol.*, x. 97, 1881; G. H. Monks, *Boston Med. and Surg. Journ.*, cxxiv. 84, 1891; Haug, *Deutsche med. Wchnschr.*, xx. 776, 1894; Stetter, *Arch. f. Ohrenh.*, xxxix. 101, 1895). Again, the ears may be obliquely inserted into the head (lower end in advance of upper); or the pinnæ may show an exaggerated or a diminished degree of curvature; or their size may be abnormally increased. The ears are often defective (crumpled, enlarged, "elephantine") in anencephalic fœtuses.

The various parts of the auricle may show anomalies, some of which are very interesting. In the *helix*, for instance, there may be defects. The Darwinian tubercle, the projection from the free posterior margin of the helix a little above the level of the crus of the antihelix, may be unusually prominent. The meaning of the Darwinian tubercle has been much debated and is not yet clear. In the so-called "Satanic ear" there is another projection than the Darwinian, situated at the highest point in the helix, and this gives to the organ a pointed and narrow appearance. Other small projections or folds in the helix may be found opposite the cymba conchæ or the fossa triangularis. The raised outline of the helix may be faintly marked or absent. Various anomalies of the *antihelix* have been reported: it may be absent, or only the inferior crus may be recognisable; the inferior crus may not be continuous with the rest of the antihelix; the main part of the antihelix may be more prominent than the neighbouring helix ("Wildermuth's ear"), and this anomaly would appear to be more common in women (Gradenigo); rarely the superior crus of the antihelix is absent; sometimes the helix and antihelix are adherent; occasionally there are accessory antihelices; and rarely there are three instead of two crura. The *lobule* may be too large or too small or absent; it may be adherent to neighbouring parts; or it may show a fissure (coloboma lobuli). The occurrence of coloboma of the lobule has a special interest from the standpoint of the question of the transmission of acquired characters: such a fissure existed in the left ear of a child whose mother's left ear had been torn accidentally by an earring (the mother being then eight years of age); the lobule of the mother's ear never properly closed; and thirteen years later she married and gave birth to eight children, of whom seven had well-formed ears and one (the second born) had the coloboma referred to (E. Schmidt, *Cor. Bl. d. deutsch. Gesellsch. f. Anthrop.*, Nov. 1888). A somewhat similar case was reported by Ornstein to the same Society as that to which Schmidt had communicated his observation; and O. Israel (*Arch. f. path. Anat.*, cxix. 240, 1890) has met with two instances in which there had been no maternal traumatism affecting the ears. B. C. Windle's paper (*Journ. Anat. and Physiol.*, xxv. 433, 1891) may also be consulted. The malformation is not to be regarded as a maternal traumatism transmitted but rather as a teratological state of the lobule arising from arrested union of the original constituent parts of the pinna. Further, in support of this view, it was noted that the artificially produced maternal fissure of the lobule and the antenatally developed coloboma of the child's ear did not correspond in the position which they occupied. Recently another case of coloboma lobuli was reported by J. Boeke (*Nederl. Tijdschr. v. Geneesk.*, ii. for 1902, p. 1034).

The *tragus* may be smaller than usual or divided into two (Talbot, *op. cit.*, p. 214); the *antitragus* may be undeveloped, or it may lie immediately opposite to, instead of below, the tragus, and so block the meatus auditorius. The *scaphoid fossa* may be prolonged into the lobule, as in an ear with three Darwinian tubercles figured by Talbot (*op. cit.*, p. 215); it may, on the other hand, be absent (especially when the antihelix is very prominent), or it may be restricted in extent. Minor malformations may also be found in the *concha.* The external auditory meatus may be double, the duplicity being caused by a septum, as in L. Guranowski's case (*Prezeglad chir.*, iv. 217, 1898).

Readers who may wish further information on this anthropological annexe (so to say) of Teratology will do well to consult the following references:—Binder, *Arch. f. Psychiat.*, xx. 514, 1888–89; H. Daae, *Norsk. Mag. f. Lægevidensk.*, 4 R., viii. 824, 1893; H. H. Ellis, *Lancet*, i. for 1890, p. 189; L. Frigerio, *Arch. de l'anthrop. crim.*, iii. 438, 1888; G. Gradenigo (many articles, including *Ann. d. mal. de l'oreille, du larynx*, xv. 279, 1889, and *Arch. f. Ohrenh.*, xxxii. 202, 1891); M. Lannois, *Arch. de l'anthrop. crim.*, ii. 336, 389, 1887; J. Julia, *Thèse*, Lyon, 1888; B. Pailhas, *Arch. di psichiat.*, xviii. 1, 1897; G. Schwalbe, *Festschrift R. Virchow*, i. 93, 1891; E. Váli, *Orvosi hetil.*, xxxv. 81, 1891; F. Warner, *Lancet*, i. for 1890, 344.

Distomus and Accessory Maxillæ.

Before I close this chapter and pass from the teratological states of the head to those of the neck, it is necessary that I refer, very briefly, to some puzzling cases which have been variously described as double-mouth (*distomus*), accessory lower jaw, supernumerary upper jaw, and teratomata of the face. These are most anomalous malformations. If they are the lowest degrees of double terata, then their discussion ought to be postponed till the double monsters are dealt with; if, on the other hand, they represent a sort of excessive formation of individual parts in a single fœtus, they are exceedingly difficult to explain by any of the known laws of teratogenesis; if they are teratomata or teratoids, then they are allied both to the double monsters and to congenital neoplasms, and become scarcely less difficult of elucidation. Oscar Israel's specimen (*Diss. inaug.*, Berlin, 1877) is one in point: it was obtained from a new-born female child who showed in the ear a double tragus and a coloboma of the lobule, and on the left side of the lower jaw a proboscis-like projection, which on removal was found to consist of a rudimentary half mandible, with tooth germs, a condyle, and a coronoid process (?), a submaxillary

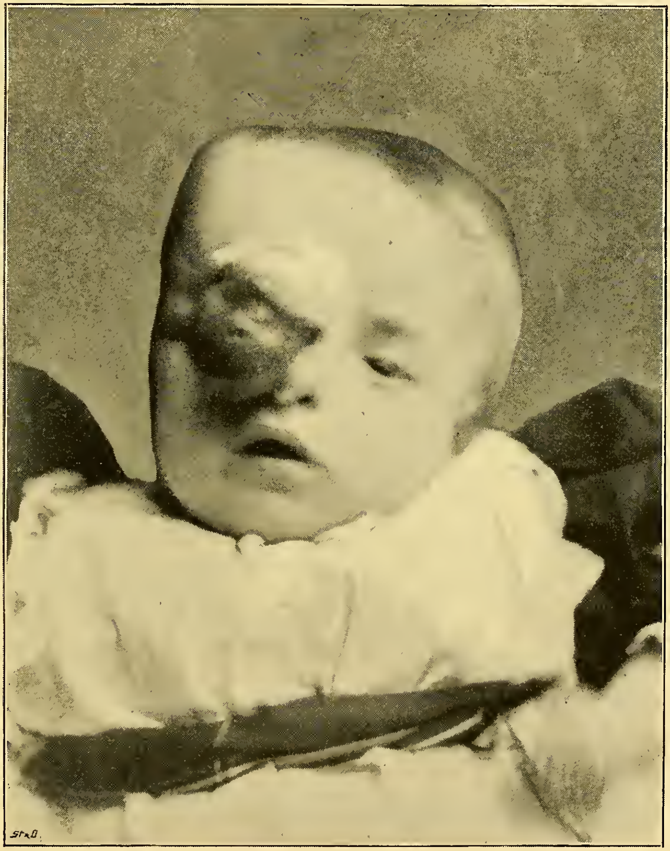

FIG. 70.—Congenital Tumour on the Face of an Infant.

gland, and a cyst. At the free extremity of this proboscis was a small round opening, supposed to be a mouth. There was also a mouth in the normal situation, which showed some asymmetry. Israel regarded his specimen as an instance of duplicity of the left half of the lower jaw. Taruffi (*op. cit.*, vi. 528) met with a somewhat similar state of affairs in an anencephalic fœtus: the nose was large and broad; the mouth was extraordinarily wide, and was turned downwards at its angles, where there was (on each side) a small opening into the buccal cavity; the lower lip in the middle line passed under the upper one, and was adherent to the palate; and on the chin was a small round opening with a reddish projection in it. In this curious case dissection showed that there were two mandibles lying side by side fused together by their inner halves. In a lamb seen by P. Gilis (*Journ. de l'anat. et physiol.*, xxxv. 707, 1899) there

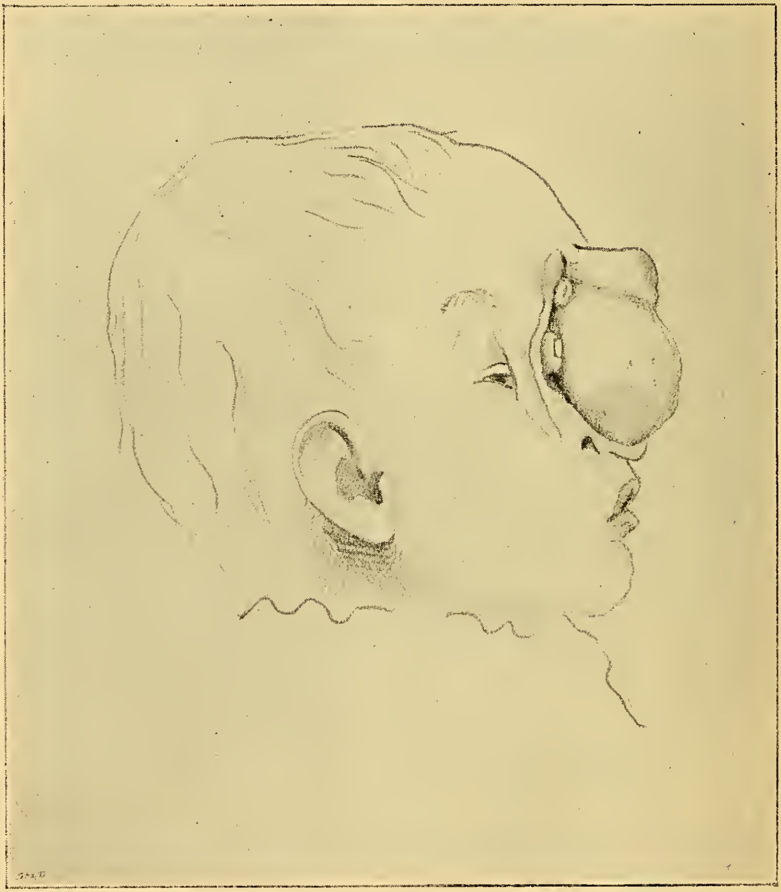

Fig. 71.—Congenital Tumour on the Face of an Infant.

were two lower jaws, four upper jaws (much reduced), and two tongues, although externally there was no trace of duplicity except in the great distance which intervened between the two eyes.

Akin to these cases was that of a congenital tumour on the face of an infant which J. Rutherford Morison asked me to examine for him in 1896 (*Trans. Edinb. Obstet. Soc.*, xxi. 254, 1896). The growth was about the size of a Tangerine orange, and appeared as if it were growing out of the right side of the nose in immediate proximity to the right eye (Fig. 70); it did not, however, communicate with the interior of the nose. On its outer aspect were two incisor teeth, which were cut at the same age (eight months) as the ordinary teeth inside the mouth (Fig. 71). Mr. Morison regarded the growth as an accessory upper jaw, and successfully operated upon it; it consisted partly of bone, partly of fibrous and mucoid tissue, and partly of hyaline cartilage. It may, on the other hand, be looked upon as a teratoma comparable to the intrabuccal growths to which the name *epignathus* has been given and which grow from the hard palate. However it be regarded, it (and the cases narrated above) must be grouped among the unsolved problems of Teratology.

CHAPTER XXIV

Merosomatous Terata (*cont.*): Malformations of the Neck: Fistula Colli; Definition; History; Varieties (Lateral, Median, Supra-hyoidean, Infra-hyoidean, Complete, Incomplete); Morbid Anatomy; Associated Malformations; Teratogenesis; Literature: Cervical Auricles: Cervical Cysts: Cystic Hygroma of the Neck: Cysts of the Thyroid and of Aberrant Thyroids: Median Fissure of the Neck: Cervical Patagium: Cervical Ribs: Malformations of the Œsophagus: Malformations of the Larynx and Epiglottis: Muscular Anomalies of the Neck.

In studying the teratological states of any region of the body it is most helpful to keep constantly before the mind's eye the embryology of that region; normal ontogenesis throwing light upon abnormal in a quite remarkable fashion. This is specially true of the cervical region; and, if the reader will take the trouble to re-read the account given (in the early chapters of this volume) of the development of the neck, or if he will at least glance at the synopsis of the organogenetic rearrangements given on pages 68 and 69, he will with much greater facility comprehend the nature and mode of origin of the malformations now to be described. The neck is the region of the branchial arches and clefts, and it follows that the malformations of the neck are mainly branchial. Thus, I shall have to refer to various projections and fistulæ (with their frequent concomitants—cysts), resulting from the imperfect closure of the branchial recesses or from anomalous budding from the arches. Further, the neck is a region which in early embryonic life can hardly be said to exist, and it is only clearly marked off when recession of the heart into the thorax is accomplished; these facts also have a bearing upon the origin of certain cervical malformations.

It has also to be remembered that in ontogenesis the lower branchial clefts open into one sinus (the precervical); imperfect closure of this sinus may lead to fistulous openings in the neck. The malformations of the cervical region have a strong resemblance to those of the ear and lower jaw, which have just been described (Chapter XXIII.); the reason is again supplied by embryology, for they are both branchial in origin. With these introductory sentences in his mind, the reader may now study with more profit the anomalies of the neck. Let us take as our type-malformation the condition known as fistula colli.

Fistula Colli.

The name *fistula colli* is given to those fistulous openings situated in the neck, either along the anterior margin of the sterno-mastoid muscle or (less commonly) in the median line, which represent imperfectly closed branchial clefts or traces of the sinus præcervicalis, and which, although insignificant in appearance, are often very difficult to close and so to cure.

Their *history* does not extend far back. C. H. Dzondi (*De fistulis tracheæ congenitis*, Halæ, 1829) was practically the first to draw attention markedly to them; but he thought they were tracheal in nature; he reported four cases. F. M. Ascherson (*De fistulis colli congenitis, adjecta fissurarum branchialium in mammalibus avibusque historia succincta*, Berlin, 1832) described eleven cases, discovered that the fistulæ were connected not with the trachea but with the pharynx, and so made clear their branchial origin; eight of the eleven individuals seen by Ascherson belonged to the same family, in three generations. Since 1832 many new observations have been made, so that the bibliography of the subject is now very large; to some of the more outstanding articles reference will be made in the text and others will be referred to at the end. It may be said that Heusinger (*Arch. f. path. Anat.*, xxix. 358, 1864) was able in 1864 to collect forty-six German observations, that J. Cusset (*Thèse*, Paris, 1877) had brought together sixty cases from French, German, and British sources, that G. Fischer (*Deutsche Chirurgie*, Lieferung 34, 1880; *Deutsche Ztschr. f. Chir.*, ii. 570, 1873) increased the number to 100, and that K. von Kostanecki and A. von. Mielecki (*Arch. f. path. Anat.*, cxx. 385; cxxi. 55, 247, 1890) increased it still further to 151. Taruffi has reported, in addition, a score of Italian observations (*op. cit.*, vii. 7, 1894).

Fistulæ of the neck may be found either at the sides or in the middle line, and they may be above or below the level of the hyoid bone. The lateral are more common than the median, and those below the level of the hyoid are more common than those above it. Apparently they are more common on the right than on the left side, for some undiscovered reason. Occasionally they are bilateral, and are then symmetrical or asymmetrical; rarely there is a fistula on one side and a cyst on the other.

Lateral fistulæ in the *supra-hyoidean* region of the neck, between the external auditory meatus and the larynx, are rare. Lannelongue and Ménard (*Affections congénitales*, i. 226, 1891) report the case of a girl, eight years of age, who showed a small fistulous opening about half an inch below the angle of the jaw on the right side, in the line of the anterior border of the sterno-mastoid muscle; a sound passed in upwards and backwards towards the ear for a distance of about an inch; a little fluid occasionally exuded from the opening. In Berg's case (*Arch. f. path. Anat.*, xcii. 183, 1883) the orifice lay a little above the thyroid cartilage on the left side, and was thought to communicate with the ear. In Virchow's specimen (dead-born infant) there was a complete fistula opening externally in the neck and internally into the pharynx; and it communicated with the external auditory canal, which was closed at the meatus (*Arch. f. path. Anat.*, xxxii. 518, 1865). In one of Heusinger's observations there was a double and symmetrical fistula in the supra-hyoidean region associated with malformations of the outer ear (*Arch. f. path. Anat.*, xxix. 358, 1864).

Lateral cervical fistulæ in the *infra-hyoidean* are commoner and more typical. They may have a free external opening and end blindly in the tissues of the neck; they may, more rarely, open freely into the pharynx, and have no external cutaneous orifice at all; or they may be complete tracts opening both externally in the neck and internally in the pharynx. A few words may be said regarding each of these varieties.

About fistulæ which open only into the pharynx, which are in fact pharyngeal diverticula, little is known. M. Watson's observation (*Journ. Anat. and Physiol.*, ix. 134, 1874–75) and Heusinger's three instances (*loc. cit.*) stand almost alone; but it is possible that some of the complete fistulæ which have been reported were at first in communication with the pharynx alone. It must always be difficult to bring forward proof that these diverticula were really antenatal in origin; at the same time there is no reason to affirm that a persistence of one or other of the embryonic pharyngeal pouches is an impossibility. Complete lateral infra-hyoidean fistulæ are also somewhat rare. It has been supposed by some that cervical fistulæ never open into the pharynx, or at least not save by the incautious use of the probe; but Bland-Sutton (*Evolution and Disease,* p. 81, 1890) has seen milk swallowed showing itself in the neck in the case of individuals whose fistulæ had never been sounded at all. G. Cavazzani (*Riforma med.*, vii. pt. 4, 31, 1891) has reported a case of complete fistula; so has M. Neuhöfer (*Med. Cor.-Bl. bayer. Aerzte,* viii. 561, 1847; *Diss. inaug.*, München, 1847).

Lateral infra-hyoidean fistulæ, which communicate only with the exterior, are the most typical and the commonest of these anomalies. The opening lies somewhere along the anterior edge of the sterno-mastoid muscle, generally not much above the level of the sterno-clavicular joint, more rarely in the neighbourhood of one side of the thyroid cartilage of the larynx. It is usually very small in size; it may lie at the top of a little eminence, or inside a depression, or may be covered by an operculum. It usually admits only the finest probe, and is explored with difficulty. A cicatrix has sometimes been found inside the pharynx, a fact which has been ascribed to closure of the internal opening of what was originally a complete fistula (H. Rehn, *Arch. f. path. Anat.*, lxii. 269, 1874). In direction, the fistula is usually ascending, towards the hyoid bone (as in a patient under the care of Dr. John Thomson, Fig. 72), or (sometimes) towards the angle of the jaw; its walls are often thick and hard; and its lumen may be irregular and may even show diverticula in various directions (H. Ribbert, *Arch. f. path. Anat.*, xc. 536, 1882). The canal varies in length from a fraction of an inch up to two or three inches. When the fistula is bilateral, it is often, but not invariably, symmetrical in position. Sometimes fibro-cartilaginous nodules lie in close proximity to the fistulous tract; these perhaps represent traces of developments in the third and fourth branchial arches similar to the cartilages of Meckel and Reichert in the first and second. These nodules have been observed by many authors, including P. Buttersack (*Arch. f. path. Anat.*, cvi. 206, 1886), S. Duplay (*Arch. gén. de méd.*, i. for 1875, p. 78; *Progrès méd.*, v. 321, 1877), and F. W. Zahn (*Deutsche Ztschr. f. Chir.*, xxii. 399, 1885). The fistulæ are lined with epithelium, columnar and sometimes ciliated in the deeper part, stratified and squamous in the outer part; the epithelium lies on a layer of connective tissue which shows many embryonic cells. A transparent secretion sometimes exudes from these fistulæ, and may irritate the surrounding skin often forming a crust over the opening; it contains columnar and squamous epithelial cells; it resembles saliva, and this resemblance caused some of the earlier observers (*e.g.* Manry) to regard the fistulæ as communicating with the salivary glands. The retention of the secretion may lead to the formation of a cyst. It may be noted that practically the only clinical character of fistulæ of the neck is the

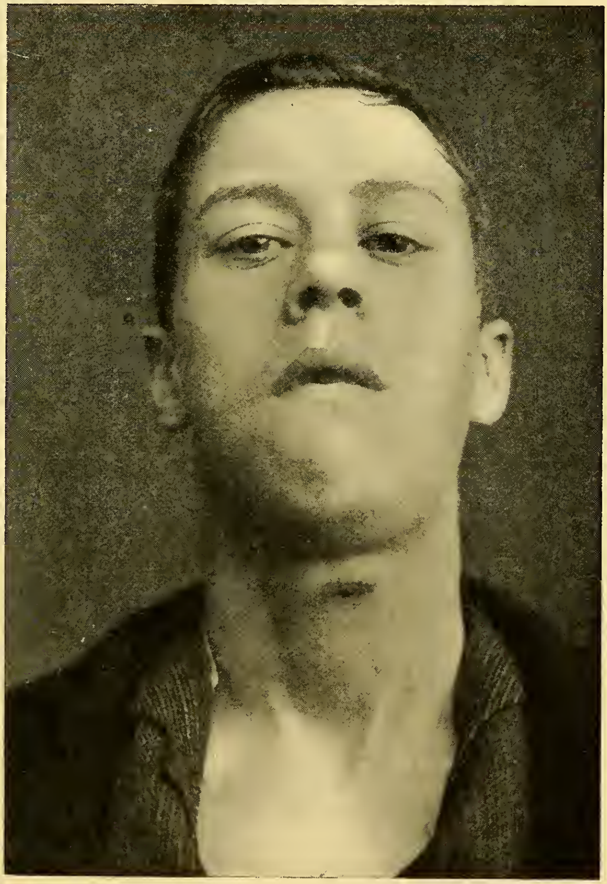

Fig. 72.—Dr. John Thomson's Case of Cervical Fistula.

secretion; and when the malformation occurs in the horse attention is commonly drawn to it by the effect of the discharge on the harness (Heusinger, *Deutsche Ztschr. f. Thiermed.*, ii. 1, 1875–76). Perhaps, also, pharyngitis is more common in such cases (Hyrtl, *Oesterr. med. Wchnschr.*, p. 53, Wien, 1842; E. Münchmeyer, *Hannov. Ann. f. d. ges. Heilk.*, n.F., iv. 12, 1844); attacks of asthma may likewise be associated (F. S. Pluskal, *Oesterr. med. Wchnschr.*, p. 902, 1846).

A comparatively common *associated malformation* of the lateral fistula colli is the cervical auricle or fibro-cartilaginous appendage; to this growth attention will be immediately directed. The same association was noted, it will be remembered, in connection with the fistula auris congenita and the preauricular appendage. The subcutaneous nodules of cartilage found sometimes in connection with the fistula have been already referred to.

Sex seems to have little or no influence on the occurrence of lateral fistulæ colli; but heredity has been shown to be a powerful factor (Ascherson, *op. cit.*; P. Oliva, *Riv. veneta d. sc. med.*, xv. 312, 1891; S. L. M'Curdy, *Columbus Med. Journ.*, ii. 244, 1883–84; A. E. Vaughan, *Brit. Med. Journ.*, i. for 1899, p. 148).

Treatment, if resolved upon, had better take the form of excision of the whole fistulous tract; but great care must be taken not to wound important structures (nervous and vascular) in the neighbourhood (G. M. Lefferts, *Med. News*, xlii. 489, 1883).

Median cervical fistulæ are rare, and above the level of the hyoid bone (supra-hyoidean) they are almost unknown. When they are present they may be discovered at any level between the hyoid bone and the manubrium sterni: thus they may be situated in the thyrohyoid space (L. Le Fort, *Bull. gén. de thérap.*, cix. 49, 1885); or under the thyroid cartilage (B. Hill, *Lancet*, ii. for 1877, p. 842); or on the cricoid cartilage (J. J. Jenni, *Schweiz. Ztschr. f. Med. Chir. u. Geburtsh.*, p. 1, 1854; Köhler, *Charité-Ann.*, iii. 433, 1878); or over the trachea (M. Roth, *Arch. f. path. Anat.*, lxxii. 444, 1878; C. Orecchia, *Osservatore*, Torino, xxxix. 289, 1888). They have characters closely similar to the lateral fistulæ, but they are very rarely complete. At first it was thought that they opened, when complete, into the laryngo-tracheal tract; but it has generally been found that the internal opening is into the pharynx. Their general direction is upwards towards the hyoid bone. The following references on median fistulæ may be consulted:—H. Luschka, *Arch. f. physiol. Heilk.*, vii. 25, 1848; R. Arndt, *Berl. klin. Wchnschr.*, xxix. 532, 1892; R. Barwell, *Trans. Clin. Soc. Lond.*, xxix. 51, 1895–96; R. Dalla Vedova, *Clin. Chir.*, vii. 828, 1899; A. Durham, *Clin. Journ.*, iii. 150, 1893–94; F. Huber, *Med. News*, lxxiii. 654, 1898; J. Bland-Sutton, *Lancet*, ii. for 1895, 1161; P. Elgeti, *Diss. inaug.*, Greifswald, 1892; M. Volkenrath, *Diss. inaug.*, Bonn, 1888.

The mode of development of cervical fistulæ (both lateral and median) has been the subject of much discussion. All writers are agreed that the lateral fistulæ are branchial in origin; but a more complete knowledge of the ontogenesis of the neck is necessary before all the varieties met with can be explained. It is known that in the human subject the branchial fissures are not really fissures but grooves; a membrane always separates the outer groove or sulcus from the inner or pharyngeal pouch. This fact makes it easy to understand the incomplete fistulæ (internal or external), but does not explain the complete, unless indeed we imagine a simultaneous arrest of the closure of both the internal and external grooves and a breaking down (or non-formation) of the septum. The position of the fistulæ, their varying length, and other characters also present difficulties not easily explained away. Perhaps some of them are got over by suggesting that the fistulæ are due not so much to want of closure of any one of the branchial grooves as of the whole sinus præcervicalis in which they are buried. The median fistula presents peculiar difficulties of its own. It may be that it too is to be regarded as due to imperfect closure of the sinus præcervicalis (with rupture of one of the occluding membranes) or to want of union of the branchial arches anteriorly; but there is another possible explanation—persistence of the thyro-glossal duct or canal of His. The last-named view is favoured by C. F. Marshall (*Journ. Anat. and Physiol.*, xxvi. 94, 1892). W. His, from his study of the ontogenesis of the thyroid gland, has established the fact that the median part of the gland is a tubular outgrowth from the ventral wall of the pharynx; this he terms the thyro-glossal duct. It consists of an upper portion leading from the foramen cæcum to the hyoid bone (lingual duct), and a lower portion from the hyoid bone to the isthmus of the thyroid (thyroid duct). If the middle part become occluded it is conceivable that persistence of one or other of the terminal portions of the canal might open anteriorly, and so cause a median fistula. Its teratogenesis cannot, however, be regarded as settled.

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Cervical Auricles.

Under the name of *branchial fibro-chondromata* or *cervical auricles* certain congenital growths on the surface of the neck have been described which have, in their structure, close affinities with preauricular appendages (*q.v. antea*). In fact the cervical auricle stands in the same relation to the fistula of the neck as the preauricular appendage does to fistula auris congenita. Many characters are common to the two growths, and it is unnecessary to describe fully the cervical appendages.

With them, as with the preauricular appendages, the influence of heredity is manifest (Reverdin's case, *Rev. méd. de la suisse rom.*, vii. 458, 1887); and one member in a family may suffer from fistula auris and preauricular appendage while another has a cervical auricle. The two growths may also exist in the same subject (L. Bernacchi, *Atti d. Assoc. med. lomb.*, i. 70, 1892). Their only clinical importance is the deformity they cause; and they may be easily removed by operation.

Their usual situation is the anterior margin of the sterno-mastoid muscle, more often low down in the neck (sterno-clavicular joint) than higher up. They have usually a core of reticular cartilage and are skin-covered; in form they tend to become pedunculated. They are usually associated with fistulæ and sometimes several of them surround such a fistula and give rise to an appearance suggesting an auricle in the neck; but the association is not constant. A good description of their histological appearances is given by E. Kirmisson (*Traité des maladies chirurgicales d'origine congénitale*, p. 168, 1898).

It is with regard to their teratogenesis and their relationship to the pendulous bodies in the necks of goats, pigs, etc., that cervical auricles have excited most interest. Bland-Sutton (*Evolution and Disease*, p. 85, 1890) has summarised much of our knowledge on these subjects. He has shown that the pendulous bodies ("pendeloques," "breloques") in the goat contain elastic cartilage like that of the pinna, that there are some small muscles attached to them, and that they are situated at spots in the neck corresponding to the points where fistulæ open. L. Blanc (*Journ. de l'anat. et physiol.*, xxxiii. 283, 1897) has fully investigated the subject of their comparative anatomy and teratology in the case of the goat, pig, and puppy; he finds that in the goat the "pendeloques" are supplied by the second cervical nerve and by a filament from the hypo-glossal, that they are not present in the goat embryo of the sixth week, and that they are, therefore, not part of the primitive branchial apparatus but something superadded. In the pig they are often associated with a cervical fistula ("canal du soyon") which Blanc regards not as an imperfectly closed branchial cleft, but as a cutaneous invagination; they are most common in autochthonous (indigenous) races, disappearing under the influence of breeding. In the embryo puppy the appendages are represented by little warts. Blanc looks upon the pendulous bodies as rudiments of a branchial ear, homologous with the pinna, and developed at the orifice of the second (?) branchial cleft. Bland-Sutton has expressed the same opinion regarding the cervical auricles in man, regarding them as of the same nature as the pendulous bodies in goats; he also points out the interesting fact that in the ancient statues and representations of fauns and satyrs there are often pendulous skin tags in the cervical region in addition to other goat-like characters (spina bifida tails, etc.). There is some doubt as to which of the branchial clefts the cervical auricle, in the human subject, is related to; but, most probably, it is to the third or fourth. A possible difficulty arises if we wish to accept the above explanation of the origin of cervical auricles: if they are really rudimentary branchial pinnæ or opercula, as Bland-Sutton and Blanc believe, then they ought to have the same origin as preauricular appendages: but it will be remembered that there was considerable doubt regarding the primitive branchial origin of these appendages; and, therefore, it would seem that the theory of the branchial origin of the cervical growths is weakened. At the same time, I think it is quite possible that the two structures may have different modes of origin. Wherever atavism is in any measure invoked in teratogenesis, difficulties of this nature arise.

Cervical Cysts.

Although cervical cysts are not malformations in the teratological sense, it may be well if I devote a few sentences to their description here. The cystic growths which occur in the neck may be of the nature of spina bifida, and to these reference has already been made (*vide* p. 292); they may be due to cystic elephantiasis, a fœtal disease described in the first volume of this MANUAL (p. 298); they may form the so-called cystic hygroma of the neck, which is closely related to cystic elephantiasis; or they may constitute branchial cysts.

Branchial cysts, as they are called, occur in the same positions in the neck as do the fistulæ, indeed their branchial origin was suspected by W. Roser (*Handbuch d. anat. Chir.*, Aufl. 3, p. 170, 1859) from a study of the fistulæ and from the topography of the cysts. They are fully described by Lannelongue and Ménard (*Affections congénitales,* i. pp. 136–210, 1891) and by C. Taruffi (*Storia della teratologia,* vii. pp. 38–59, 1894), and to their works I refer the reader for full details. The most generally accepted theory of origin of these cysts is the persistence of some of the epithelium lining the branchial clefts or grooves after the clefts themselves have closed; although shut in, the epithelium continues to grow and so initiates a cyst. Attempts have been made to group the cysts according to the branchial fissure from which they arise, but without complete success; the best classification yet available is the topographical or regional one. Thus there are median cysts lying above the level of the hyoid bone and often known as sublingual dermoid cysts or as supra-hyoidean dermoids; others are lateral in position although supra-hyoidean, and of these I met with an example by accident when making a coronal frozen section of the head of a fœtus (*vide* Fig. 19 in the first volume of this MANUAL). Others are median and infra-hyoidean, being either thyro-hyoidean or infra-laryngeal; and yet others are infra-hyoidean but lateral in position. All these cysts, as a rule, consist only of one cavity; they are generally rounded, less often cylindrical; they are nearly always superficial; the cavity is most commonly lined by stratified squamous epithelium like that of the skin, sometimes with papillæ, hairs, hair-follicles, and sebaceous and sudoriparous glands; less often it is lined by columnar ciliated epithelium; and the contents vary much, being sometimes mucus, sometimes serum, and most often an atheromatous material containing degenerated epithelial cells. As we shall see immediately, these characters are quite different from those met with in hygroma of the neck. From their mode of origin it is not to be expected that all cervical cysts will be present at birth although some are; it is quite easily understood that the functional activity of the buried epithelium may not have long enough time or be great enough to produce a cyst in antenatal life. The differences in the character of the epithelium lining the cysts have been explained by supposing that in some of them the included epithelium came from the outer (cutaneous) aspect of the neck and in others from the internal (pharyngeal) aspect.

Cystic hygroma of the neck (hygroma cysticum congenitum colli) differs in several respects from the true branchial cysts. They are apparently not so often met with: I have seen only one case in 327 instances of antenatal morbid states, that shown in Fig. 73, an infant born in the Maternity Hospital, Edinburgh, in Dr. Underhill's quarter in May 1900. They are often deep seated, and even when apparently superficial are apt to have diverticula passing far in among the important vessels and muscles of the neck. They are often large enough at birth to cause serious delay in labour, and may fill up all the space between the angle of the jaw and the chin above and the upper end of the sternum inferiorly. They have usually a quite irregular outline and an elastic consistence; and they are made up of several cyst-cavities. The lining membrane is an endothelium, like that of a lymphatic vessel, and their contents are generally clear serum, which may sometimes be brownish in colour as the result of hæmorrhage into the cyst. In all these respects the hygroma colli differs from the branchial cyst. Its treatment is often very difficult, for complete excision involves prolonged dissection among vascular and nervous structures which may easily be wounded; perhaps, in many cases, the best plan is to open the cyst, break down the septa between the loculi, and stitch the cyst wall to the edges of the skin incision (marsupialisation). With regard to its origin, various opinions have been advanced. It cannot always be associated either with the salivary glands or the intercarotid ganglion, for it may be situated far from both these structures. There are no sufficient reasons for looking upon it as of the nature of an angioma, and the only satisfactory theory is that it is due to an anomaly of the lymphatic system (Lannelongue and Ménard, *op. cit.*, i. 632, 1891). Cystic enlargements of the thyroid gland occur, but they are distinct from cystic hygroma. It is then, in all probability, to be considered as a lymphangioma; and it is, therefore, related to the fœtal disease known as general cystic elephantiasis, which has been described in the first volume of this MANUAL (p. 297).

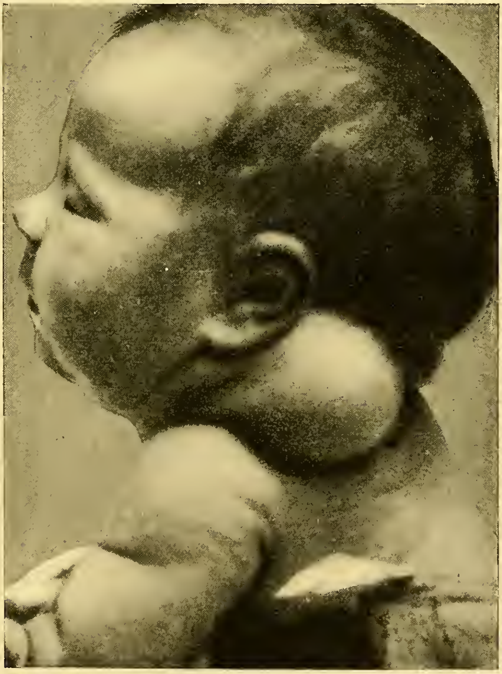


FIG. 73.—Cystic Hygroma of the Neck. Case No. 254.

Cystic enlargement of the thyroid gland may cause a congenital swelling in the neck. Such growths are usually regarded as constituting one of the varieties of congenital goitre (*struma congenita*), a morbid state already described in Vol. I. (p. 374). They are to be looked upon as fœtal diseases rather than as embryonic malformations, and, therefore, do not fall to be considered here. The closely allied cysts developed in aberrant lobules of the thyroid (supra-hyoidean, hyo-thyroidean, intra-laryngeal, and intra-thoracic) have more claim to be regarded as teratological, for they take origin in structures which ought, in all probability, entirely to disappear. An interesting account of them is to be found in Taruffi's *Storia della teratologia*, vii. pp. 76–105, 1894; Bland-Sutton also describes them fully in his work on Tumours (3rd ed., p. 366, 1903). Many bibliographical references are in the *Index Catalogue* (Washington) under the heading "Cysts and Cystic Tumours of the Neck" (vol. ix. 665, 1888).

Median Fissure of the Neck.

When we consider the comparative frequency of failure of union of the abdominal walls in the middle line it is a little surprising to find that in the cervical region a similar failure is very rare. Median fissure of the neck (*tracheloschisis* or *schistocormus fissicollis*) is among the rarest of teratological states, and when it occurs it is associated with upward displacement of the heart. G. Breschet (*Répert. gén. d'anat. et physiol. path.*, ii. 1, 1826) has, for instance, reported the case of a new-born infant in which the heart, lungs, and thymus gland were all extra-thoracic and lay in the neck above the clavicles and under the jaw. The two halves of the lower jaw were separated from each other, the apex of the heart lying between them and being attached to the tongue. From the base of the heart the aorta took origin and passed directly into the thorax. A somewhat similar displacement of the heart (named by Breschet "cephalic ectopia cordis") has been seen in the lamb (C. Weese, *Diss. inaug.*, Berolini, 1818). Another form of median fissure of the neck is associated with displacement downwards of the tongue (*tracheal ectopia of the tongue*). This teratological state is also of extreme rarity, almost the only known instance being that described and figured by Ahlfeld (*Die Missbildungen des Menschen*, p. 167, 1882; *Atlas*, plate xxviii. figs. 16, 17); it was that of a fœtus of four or five months, in which the whole floor of the mouth was wanting and the tongue was displaced downwards into a vertical fissure in the neck. K. Kostanecki has met with a somewhat similar state in the chick (*Arch. f. path. Anat.*, cxxiii. 427, 1891), and is of opinion that such malformations are not due to defects in closure of the branchial clefts, but represent the persistence of the more primitive arrangement in which there is a wide mesobranchial space in which lies the tuberculum impar of the future tongue.

Cervical Patagium.

I have already (p. 183) referred to the weblike structure (*patagium*) which may be found stretching from the neck to the shoulder on one or both sides, as in O. Kobylinski's case (*Arch. f. Anthrop.*, xiv. 343, 1883). Bland-Sutton (*Evolution and Disease*, p. 143, 1890) places these weblike expansions among the instances of spurious atavism, and refuses to see in them any attempt to reproduce in the human subject the parachute of flying mammals or the wings of birds. I quite agree with him. Possibly the patagium may be due to amniotic pressure which keeps adjacent parts of the body abnormally in contact during development; but it must be admitted that there is a degree of mystery about it in whatever part of the body it may be found. To regard it as a "spontaneous variation or sport" (Bland-Sutton) does not throw much light upon it.

Cervical Ribs.

Supernumerary ribs may be met with in the lumbar or in the cervical region, but those in the latter locality have the greatest clinical importance. It is seldom that a cervical rib is observed at the time of birth, indeed they are not recognised, as a rule, till the individual has reached the age of between fifteen and twenty years. I have had an opportunity of examining one patient with this deformity: she was a girl of twenty-two, under the care of Dr. James in the Edinburgh Royal Infirmary, and, in addition to a cervical rib on each side, she had an imperforate condition of the vagina with distension of the uterus. I examined her in April 1899.

As a rule, the cervical rib is attached to the transverse process of the seventh cervical vertebra; it may be present on one side only, but is more often bilateral, although never exactly symmetrical. Rarely there are two supernumerary ribs on the same side (M. Borchardt, *Berl. klin. Wchnschr.*, xxxviii. p. 1265, 1901). The rib usually ends freely or is united to the first true rib; it is rarely supplied with a cartilage, and still more rarely reaches the sternum. Sometimes it is a mere rudiment consisting of little more than the head.

Cervical ribs may be met with in some mammals as well as in the human subject. Thus they have been found in the dog (W. Gruber, *Arch. f. Anat. Physiol. u. wissensch. Med.*, 542, 1867; S. Puchkovski, *Uchen. Zapiski Kazan. Vet. Inst.*, xiii. 227, 1896), in the sheep, in the horse (C. Taruffi, *Mem. Accad. d. sc. di Bologna*, 3 s., x. 92, 107, 1879), and in the whale (W. Turner, *Journ. Anat. and Physiol.*, iv. 130, 1869–70; v. 348, 1870–71; xvii. 384, 1882–83). They are generally regarded as an atavistic phenomenon, it being supposed that the seventh cervical vertebra was originally supplied with a pair of ribs.

No symptoms may result from the presence of cervical ribs; on the other hand, curious nervous and vascular phenomena may occur, which are apparently due to the pressure exercised by the rib upon the subclavian artery, the brachial plexus, and the cervical sympathetic system. The circulation in the arm of the same side as that on which the rib lies becomes disturbed, the limb is white, or may show appearances like those in Raynaud's disease; various nervous anomalies, such as neuralgia, hyperæsthesia, and deficient nutrition of the nails may also be noticed. A good description of the clinical phenomena which may be associated with cervical ribs is given by T. E. Gordon (*Brit. Med. Journ.*, i. for 1901, p. 1395); in his opinion many of the results may be due to pressure exercised by the rib not at its distal but at its proximal end. The anomaly may be well demonstrated by the Röntgen rays. Operative interference may be required on account of the severity of the symptoms; and it is well for the surgeon to bear in mind that the pleural cavity of the same side may be abnormally prolonged upwards into the root of the neck.

The anomaly has been known since the time of Vesalius, and many observations have been made, one hundred and fourteen of which were collected by C. Engel (*Ueber Halsrippen beim Menschen*, München, 1887). I append some bibliographical references.

(1) H. E. Clark, *Glasgow Med. Journ.*, 5 s., vi. 361, 1874. (2) S. F. Clark, *Brit. Med. Journ.*, ii. for 1895, p. 1162. (3) E. Coues, *Science* (Cambridge), iii. 61, 1884. (4) Danlos, *Bull. et mém. Soc. méd. d. hôp. de Paris*, 3 s., xiv. 845, 1897. (5) A. Dymock, *Edinb. Med. and Surg. Journ.*, xl. 304, 1833. (6) E. Ehrich, *Diss. inaug.*, Rostock, 1895. (7) Gillette, *Bull. Soc. anat. de Paris*, xliv. 72, 1869. (8) L. E. Hertslet and A. Keith, *Journ. Anat. and Physiol.*, xxx. 562, 1895–96. (9) R. Hirsch, *Wien. klin. Rundschau*, ix. 793, 1895. (10) Huntemüller, *Ztschr. f. rat. Med.*, 3 R., xxix. 149, 1867. (11) C. Jewett, *Ann. Anat. and Surg. Soc.*, i. 101, 1878-79. (12) A. Lane, *Guy's Hosp. Rep.*, xlii. 109, 1883–84. (12*a*) H. Leboucq, *Ann. Soc. de méd. de Gand*, lxiv. 34, 1885. (13) R. W. Reid, *Proc. Anat. Soc. Gr. Brit. and Ireland*, p. iii., 1889–90. (14) Resegetti, *Gazz. med. di Torino*, xlvii. 207, 1896. (15) G. Romiti, *Giorn. internaz. d. sc. med.*, ii. 674, 1880. (16) F. J. Shepherd, *Amer. Journ. Med. Sc.*, clxix. 112, 1883. (17) H. J. Stiles, *Trans. Med.-Chir. Soc. Edinb.*, n.s., xv. 54, 1896. (18) Stifler, *München. med. Wchnschr.*, xliii. 445, 1896; (19) L. Stieda, *Arch. f. path. Anat.*, xxxvi. 425, 1866. (20) J. C. Warren, *Boston Med. and Surg. Journ.*, cxxxiv. 258, 1896. (21) H. Alderson, *Brit. Med. Journ.*, ii. for 1897, p. 1638. (22) L. Grounauer, *Rev. méd. de la suisse rom.*, xviii. 19, 1895. (23) H. L. Barnard, *Clin. Journ.*, xxiii. 190, 1903–04. (24) Knoch, *Deutsche mil.-ärztl. Ztschr.*, xxxii. 59, 1903. (25) E. Ranzi, *Wien. klin. Wchnschr.*, xvi. 274, 1903. (26) R. Menocal, *Semana méd.* (Buenos Aires), x. 269, 1903. (27) A. Weissenstein, *Wien. klin. Rundschau*, xvii. 373, 394, 1903.

Malformations of the Œsophagus.

Although the œsophagus is only in part a cervical organ, it will be convenient to refer here to its malformations. These may be enumerated as follows:—(1) Complete absence of the œsophagus, its place being taken by a thin muscular band stretching from the pharynx to the cardiac end of the stomach; (2) termination of the œsophagus in a simple cul-de-sac; (3) termination of the œsophagus in a cul-de-sac, the lower rudiment of the canal communicating with the trachea or bronchi; (4) tracheo-œsophageal fistula, the œsophagus being otherwise normal; (5) membranous obstruction of the œsophagus; (6) presence of œsophageal diverticula; and (7) duplicity of the œsophagus. All these anomalies are rare, with the exception of the third; I, therefore, choose this as the type for special description.

Congenital imperforation of the œsophagus, as it is called, is indicated by no external signs. The infant thus affected may be born prematurely, but as a rule it comes at the full term, and is plump and well nourished. No surprise need be felt on this account, the umbilical vein and not the œsophagus being, as we know, the gullet of the fœtus. When the infant is put to the breast it is soon evident that something is wrong: the milk is returned with or without violent vomiting, there is coughing, the face is congested, and it seems as if suffocation is impending; but the attack soon passes off; then the child again takes the breast, only to reproduce the same series of alarming phenomena. No anomaly is found in the mouth, the breathing is not affected, and it is only when the physician tries to pass a bougie into the stomach that the œsophageal imperforation is discovered. The rest of the clinical history of the case may be summarised as rapid emaciation and death usually within the first week. Some meconium may be passed from the bowels, and some nourishment may reach the infant in the form of nutrient enemata, but the fatal issue invariably comes. No operative interference yet devised is applicable, and the cause is evident when we consider the morbid anatomy of such cases.

The pharynx ends, as a rule, a little below the level of the cricoid cartilage in a blind extremity showing sometimes a slight dilatation. There may be no œsophageal canal below this point; but it is more common to find an œsophageal rudiment passing upwards from the cardiac end of the stomach and ending blindly at the level of the bifurcation of the trachea. From this lower or gastric part of the œsophagus a small opening establishes a communication with the trachea, so that a sound passed from the stomach into the œsophageal pouch emerges in the air passages. The tracheo-œsophageal fistula is a practically constant arrangement, whose meaning has not been discovered; but its presence explains how it is that small quantities of milk may be found in the stomach in some of these cases—the fluid has regurgitated from the upper œsophageal sac into the mouth, it has then found its way into the larynx and trachea, and thence through the fistula into the lower end of the œsophagus and so into the stomach. Sometimes a band of muscular fibres, lying posterior to the trachea, has been traced from the upper pharyngeal to the lower œsophageal pouch. Normal stratified squamous epithelium has been found in both the upper and the lower pouches; and while striped muscular fibres have been noted in the upper part, only unstriped have been seen in the lower (H. von Luschka, *Arch. f. path. Anat.*, xlvii. 378, 1869).

Associated malformations are uncommon, but have sometimes been noted. Thus Polaillon (*Bull. et mém. Soc. de chir. de Paris*, n.s., i. 613, 1875) has recorded a case of anal imperforation with recto-urethral fistula, with absence of radius and club-hands, in addition to an imperforate state of the œsophagus. In G. M. Davis' case there was also imperforate anus (*London Med. Gaz.*, xxxi. 543, 1842–43); in J. de Bary's there was transposition of the viscera (*Arch. f. path. Anat.*, xxxi. 430, 1864); and in O. Ward's there was an open foramen ovale and ductus arteriosus (*Trans. Path. Soc. Lond.*, viii. 173, 1856–57). Graver defects and monstrous states may be met with, *e.g.* pseudencephaly (Pinard, *Bull. Soc. anat. de Paris*, xlviii. 685, 1873).

Very little is known regarding the causation and teratogenesis of imperforation of the œsophagus. It has been found associated with hydramnios and with fibro-fatty changes in the placenta (C. Périer, *Bull. Soc. de chir. de Paris,* 3 s., ii. 587, 1873; *Bordeaux méd.*, iii. 75, 1874; F. Boisvert, *Journ. de méd. de Bordeaux,* xvi. 125, 1886–87); but it is difficult to see any connection between these states and the œsophageal anomaly, unless, indeed, it be maintained that the excess of liquor amnii is due to the fœtus being unable to swallow that fluid. It is to be noted that this teratological state is not to be confused with imperforation of the pharynx such as occurs in agnathus and otocephalus; that is the persistence of a normal phase of development (*vide* p. 30), while imperforation of the œsophagus, so far as is known, is not. It is remarkable that it is practically constant in its position (level of lower end of trachea) and that the gastric portion of the œsophagus should always open into the trachea; from these two circumstances some light upon its teratogenesis ought to shine forth, but if there be any rays they are of a kind invisible to the eye of the teratologist and embryologist. It is possible that the fistula between the trachea and the œsophageal pouch may be the means by which liquor amnii reaches the stomach and intestines in the antenatal life of these deformed infants; at any rate it is commonly reported that they pass meconium during the first few days of life. It may be added that the tracheo-œsophageal fistula may exist without imperforation (Tarnier, *Bull. Soc. de chir. de Paris,* 2 s., ii. 475, 1873).

A very typical case of imperforate œsophagus was shown to me by Dr. John Thomson in 1899; it was afterwards fully reported by him (*Trans. Med.-Chir. Soc. Edinb.*, n.s., xviii. 112, 1899). Several other observations are on record, among which I may refer the reader, interested in collecting references, to the following:—

(1) T. Annandale, *Edinb. Med. Journ.*, xiv. 598, 1868–69. (2) P. B. Ayres, *Trans. Path. Soc. Lond.*, iii. 91, 1850–52. (3) Boucher, *Bull. Soc. anat. de Paris,* xliii. 127, 1868. (4) F. Brentano, *Bull. Soc. anat. de Paris,* 5 s., viii. 638, 1894. (5) C. K. Bowes, *Brit. Med. Journ.*, i. for 1897, p. 586. (6) W. Brüel, *Diss. inaug.*, Giessen, 1892. (7) J. Houston, *Dublin Hosp. Rep.*, v. 310, 1830. (8) L. Lehmann, *Nederl. Tijdschr. v. Geneesk.*, 2 R., iv., 2 Afd. 142, 1868. (9) C. E. Levy, *N. Ztschr. f. Geburtsk.*, xviii. 436, 1845. (10) T. Mellor, *Lond. Med. Gaz.*, xxvi. 542, 1840. (11) J. W. Ogle, *Trans. Path. Soc. Lond.*, vii. 52, 1855–56. (12) Padieu, *Bull. Soc. anat. de Paris,* x. 95, 1835. (13) Pagenstecher, *Journ. f. Geburtsh.*, ix. 113, 1829. (14) E. Porro, *Ann. univ. di med.*, ccxvii. 421, 1871. (15) Schoeller, *N. Ztschr. f. Geburtsk.*, vi. 264, 1838. (16) Sonderland, *Journ. compl. du dict. d. sc. med.*, viii. 369, 1821. (17) F. E. Sundewall, *Upsala Läkaref. Forh.*, v. 385, 1869–70. (18) Willett, *Trans. Path. Soc. Lond.*, xlv. 78, 1894. (19) B. van de Water, *Diss. inaug.*, Leyden, 1857. (20) Morell Mackenzie, *Manual of Diseases of the Throat and Nose*, ii. 218, 1884 (Full Bibliography).

Congenital narrowness of the œsophagus, with or without an œsophageal diverticulum, constitutes an anomaly which cannot be absolutely affirmed to be antenatal in origin unless it be met with at birth, and since it does not prevent postnatal life (as does imperforation of the œsophagus) it is seldom that it is discovered at an early age.

Malformations of the Larynx.

Malformations have rarely been reported; but it is not safe to conclude that they are therefore less common than many other anomalies. Probably many of them pass unrecorded because undiscovered (*e.g.* in stillborn infants).

A typical instance of *imperforation of the larynx* was met with and reported by J. Cousin (*Loire méd.*, xviii. 44, 1899). It was in a well-formed male infant, born with the help of forceps. The child made inspiratory efforts, but it could be seen that he did not respire, although he was really living and moving his arms and legs. His skin remained white. The heart continued to beat, so after ordinary efforts at resuscitation had been made with no success, an attempt was instituted to introduce the insufflator of Ribemont into the larynx. It was then discovered that there was an imperforate condition of the larynx; the epiglottis was completely ossified and adhered in its whole circumference to the subjacent cartilage. The infant died twenty minutes after birth. A tracheotomy would have been necessary to have assured the establishment of respiration, and further interference would doubtless have been required to keep the child in life.

Narrowing of the glottis has been described by several writers; it is nearly always due to a tense membrane stretching between the vocal cords; and this membrane, fibrous in nature, begins at the anterior commissure of the glottis and ends posteriorly in a semicircular margin. Cases have been reported by T. A. de Blois (*Trans. Amer. Laryngol. Assoc.*, vi. 42, 1884), O. Chiari (*Wien. klin. Wchnschr.*, x. 607, 1897), L. Elsberg (*Trans. Amer. Med. Assoc.*, xxi. 219, 1870), P. Fraenckel (*Deutsche med. Wchnschr.*, xxviii. 909, 1902), M. Mackenzie (*Trans. Path. Soc. Lond.*, xxv. 35, 1873–74), G. V. Poore (*Trans. Internat. Med. Congr.*, 7 sess., London, iii. 316, 1881), G. Scheff (*Allg. Wien. med. Ztg.*, xxiii. 280, 289, 1878), and by F. Sippel (*Med. Cor. Bl. d. Württemb. ärztl. Ver.*, lxxiii. 133, 1903). The clinical manifestation of this malformation is complete aphonia; to cure this, tracheotomy has been performed; and thereafter bougies have been passed through the larynx by the tracheal wound with good success in P. Bruns' case (*Arch. f. Laryngol. u. Rhinol.*, i. 25, 1893).

Various *anomalies of the epiglottis* have been, from time to time, put on record, such as absence or duplicity (F. Donaldson, *New York Med. Journ.*, xliv. 149, 1886; T. R. French, *Ann. Anat. and Surg. Soc.*, ii. 271, 1880; etc.); but special interest attaches to the question whether congenital laryngeal stridor in infants is due to some structural anomaly of the upper end of the larynx or to ill coordinated spasmodic action of the muscles of respiration. J. Thomson and A. Logan Turner (*Brit. Med. Journ.*, ii. for 1900, p. 1561) favour the latter view; but according to others the epiglottis is malformed, being folded together, and herein is the cause of the stridor (H. Refslund, *München. med. Wchnschr.*, xliii. 1182, 1896; D. B. Lees, *Trans. Path. Soc. Lond.*, xxxiv. 19, 1883; P. Bruder, *Stridor larynyé congénital des nourrissons*, Paris, 1901). As the child grows older and the larynx becomes firmer the malformation and the stridor disappear.

Muscular Anomalies of the Neck.

Various muscular anomalies of the neck are met with (Veau, *Bull. Soc. anat. de Paris*, 5 s., vii. 168, 1893). Absence of the left sterno-mastoid in a case complicated by oligohydramnios was put on record by Jaggard (*Amer. Journ. Obstet.*, xxix. 433, 1894), while Thomas (*Brit. Med. Journ.*, ii. for 1894, p. 1178) noted an instance of absence of the left complexus producing pseudo-torticollis. There may be unilateral defect of the platysma myoides (E. Remak, *Neurol. Centrlbl.*, xiii. 248, 1894), and the digastric muscle may show anomalies (H. Morestin, *Bull. Soc. anat. de Paris*, 5 s., viii. 653, 1894; Siraud, *Province méd.* (Lyon), ix. 219, 1895). E. Juvara described a thyro-glandular muscle in the neck (*Bull. Soc. anat. de Paris*, 5 s., viii. 728, 1894), and L. Wilmart reported an anomalous auriculo-stylo-glossus (*Journ. de méd. chir. et pharmacol.*, p. 788, 1895). Many other instances might be cited.

CHAPTER XXV

Merosomatous Terata (*cont.*): Malformations of the Thorax: Anomalies of the Clavicle (Absence, Incomplete Development, Bifurcation); Anomalies of the Scapula (Foramina, Projections, Elevation); Anomalies of the Ribs (Bifurcation, Incomplete Formation); Anomalies of the Mammary Glands (Absence, Hypoplasia, Athelia, Polymastia); Anomalies of the Muscles (Pectoralis, Sternalis, Trapezius, etc.); Congenital Diaphragmatic Hernia, Illustrative Cases, Varieties, Clinical Characters, Morbid Anatomy, Teratogenesis, Literature; Malformations of the Sternum; Fissure of the Sternum; Ectopia Cordis; Pleurosomus.

MALFORMATIONS of the thorax include those of the osseous and muscular framework of the chest as well as of its contained organs. They constitute a group of very diverse anomalies related to each other almost solely by regional proximity. In this chapter I shall study the teratological states of the thoracic framework, and in the next the malformations of the viscera.

Malformations of the Clavicle.

Absence or defective development of the clavicle has rarely been recorded. One of the bones may be entirely absent (P. Niemeyer, *Tagebl. d. Versamml. deutsch. Naturf. u. Aerzte*, Hannover, xl. 68, 1865); but entire absence of one or both clavicles would appear to be rarer than incomplete development. The form which the latter anomaly takes is absence or non-ossification of the outer or acromial end of the bone, which has the clinical effect of allowing the shoulders to be closely approximated in front of the thorax. L. H. D. van den Bussche (*Diss. inaug.*, Freiburg, 1890) described the case of a man who was quite ignorant of his malformation and yet had bilateral absence of the corpus and acromial part of the clavicle; the state of the platysma, pectoralis major, deltoid, trapezius, sterno-mastoid, omohyoid, rhomboideus, and serratus anticus muscles was found to agree with the osseous defect (*e.g.* the clavicular part of the sterno-mastoid was poorly developed). N. Giannettasio's patient (*Arch. di ortoped.*, xvi. 65, 1899) was a man, fifty-four years of age; his clavicles were represented by two sternal fragments, the ends of which, instead of reaching the scapula, floated free among the soft parts of the supra-clavicular triangle. A similar condition of the shoulder girdle was noted by C. Gegenbaur (*Jenaische Ztschr. f. Med. u. Naturw.*, i. 1, 1864) in a woman who had been twice married and who had had children similarly affected by both husbands. Heredity was also evident in

G. Carpenter's case (*Lancet*, i. for 1899, p. 13), in which a little girl, her father, and a brother had defective development of the clavicle. A striking feature of all these cases is the small amount of inconvenience which the deformity seems to have caused (G. Schorstein, *Lancet*, i. for 1899, p. 10). Little is known of the teratogenesis of the condition: the clavicle is a peculiarly human possession and it is also the first bone in the body to ossify, therefore atavism or arrested development or both may be invoked; on the other hand, fœtal rickets in the second month of antenatal life has been alleged. J. Comby (*Traité des maladies de l'enfance*, 2nd edit., i. 973, 1904) adopts for this malformation the name *cleido-cranial dysostosis* (proposed by Marie and Sainton in 1897); it is true that cranial deformities have frequently been found associated with clavicular defect, and that these take the form of persistence of the fontanelles (pseudo-hydrocephalus); but it does not seem that the association is sufficiently constant to establish a new name for the malformation, nor to throw much light upon its mode of origin. If it is as rare as the records would lead us to suppose, it is remarkable how many cases have been reported during the past few years. I append some references in addition to those already mentioned: G. Scheuthauer, *Allg. Wien. med. Ztg.*, xvi. 293, 301, 309, 1871; O. Kappeler, *Arch. d. Heilk.*, xvi. 265, 1875; F. Stahmann, *Ztschr. f. Med. Chir. u. Geburtsh.*, xi. 433, 1857; T. S. Dowse, *Trans. Path. Soc. Lond.*, xxvi. 166, 1875; A. Guzzoni degli Ancarani, *Boll. scient.*, Pavia, ix. 72, 1887; Todd, *St. Louis Cour. Med.*, xix. 373, 1888; K. Preleitner, *Wien. klin. Wchnschr.*, xvi. 70, 1903; H. M. Sherman, *Amer. Med.*, v. 569, 1903; A. Gross, *München. med. Wchnschr.*, l. 1151, 1903.

Bifurcation of the clavicle would appear to be excessively rare, but E. H. Bennett (*Dublin Journ. Med. Sc.*, lvi. 413, 1873; lx. 166, 1875) has recorded a case in which the bone had two articulations with the scapula of the same side, the coraco-clavicular joint being very imperfect. In A. de Giovanni's observation (cited by Taruffi, *Storia della teratologia*, vii. 160, 1894), a projection passed from the body of the right clavicle upwards in the neck to join the vertebral column between the fifth and sixth cervical vertebræ.

Malformations of the Scapula.

Congenital *foramina* in and *projections* from the scapula have from time to time been reported (W. Gruber, *Arch. f. Anat. Physiol. u. wissensch. Med.*, 300, 1871; *Arch. f. path. Anat.*, lxix. 387, 1877); the suprascapular notch may exist as a foramen; and there may be a separate acromion process (Struthers and Ronaldson, *Trans. Med. Chir. Soc. Edinb.*, xv., Appendix i. pp. 42, 52, 1896). Within the last decade, however, *congenital elevation of the scapula* may be said to have attracted more attention to itself than all the other anomalies of that bone. This deformity seems first to have been described by M'Burney in 1888 (*New York Med. Journ.*, xlvii. 582, 1888), but it was more particularly brought before the profession by Sprengel in 1891 (*Arch. f. klin. Chir.*, xlii. 545, 1891), and has been sometimes called "Sprengel's deformity" in consequence. It consists in the abnormally high position occupied by one scapula, usually the left; there is close approximation of the upper border of that bone to the clavicle of the same side, so that the supraclavicular space is abolished; and the lower angle of the bone is drawn closer to the vertebral column, a character which distinguishes this anomaly from the upward displacement of the shoulder blade seen in scoliosis. Although usually unilateral, the deformity may be bilateral (J. G. Milo, *Nederl. Tijdschr. v. Geneesk.*, 2 R., d. 2, 695, 1897). In some cases a cartilaginous or osseous bar has been felt passing from the scapula towards the seventh cervical vertebra (E. Kirmisson, *Traité des maladies chirurgicales d'origine congénitale*, p. 490, 1898; J. H. Waterman, *Arch. Pediat.*, xix. 455, 1902). Associated malformations may be met with, such as defect of the pectoralis major muscle (L. Wolffheim, *Ztschr. f. orthopäd. Chir.*, iv. 196, 1896), absence of radius (Bolten), and anal atresia and ectopia (Kirmisson). The sister of one of G. Joachimsthal's patients suffered from congenital dislocation of the hip joint (*Die angeborenen Verbildungen der oberen Extremitäten*, Hamburg, 1900). In passing I may say that the reader will find a good account of this scapular anomaly with a bibliographical list in Joachimsthal's work above mentioned.

As might be expected, considerable mystery surrounds the origin of congenital elevation of the scapula. Some authors (*e.g.* Schlange, *Deutsche med. Wchnschr.*, xvii. 1383, 1891) have placed it in the same category with torticollis as a result of primary muscular defects; others (*e.g.* M'Burney, *loc. cit.*) looked for an intranatal cause, such as traumatism during labour; others (*e.g.* Kirmisson, *op. cit.*) suspected a malformation of the scapula, a suspicion strengthened by one of Bar's specimens examined by Kirmisson; and yet others (Sprengel, *loc. cit.*; J. Bolten, *Münchn. med. Wchnschr.*, xxxix. 671, 1892) found it in deficient quantity of liquor amnii and dorsal displacement of the arm during fœtal life. It may be said, therefore, that there is a postnatal, an intranatal, and two antenatal theories of this abnormality. With regard to the antenatal hypothesis, that which regards it of fœtal origin is supported by the facts that deficiency of the liquor amnii has actually been observed, and that the arms tend to be dorsally displaced after birth in some instances. In a case of labour at the Royal Maternity Hospital (Edinburgh) during last winter (1903–04) I had my attention drawn to a case in which the left scapula of the fœtus could be very distinctly felt through the maternal abdominal walls; so marked was the displacement and prominence of the bone that we expected to find Sprengel's deformity at birth, but there was no sign of it, although, of course, it may possibly have developed later. The theory that the high elevation of the shoulder is sometimes at least of embryonic origin is supported by the association of the deformity with undoubtedly embryonic defects, such as absence of the radius, and by the presence of scapular malformations (bar passing to spinal column, etc.). We are, therefore, warranted in placing it among the embryonic malformations, although there is no certainty that some cases may not be due to anomalies arising in fœtal life or even during and immediately after labour. It may be added that spinal scoliosis appears to be sometimes associated with it simply as a complication.

Treatment has consisted generally of gymnastics, and occasionally resection of the exostosis passing from the scapula to the vertebral column has been performed.

Malformations of the Ribs.

Various anomalies affecting the ribs may be met with. I have already referred to supernumerary ribs in the region of the neck (cervical ribs), but an additional rib may also occur in connection with the first lumbar vertebra (C. B. Lockwood, *Trans. Path. Soc. Lond.*, xxxvi. 359, 1884–85). Two-headed or *bicipital* ribs are also occasionally discovered, generally in the dissecting room; the commonest rib to show this anomaly is the first, and there is sometimes a doubt whether it represents a fusion of a cervical rib with the first thoracic or of the first with the second thoracic ribs. Several interesting contributions to our knowledge of these bicipital ribs have been made by Sir William Turner (*Journ. Anat. and Physiol.*, xvii. 384, 1882–83), W. Gruber (*Arch. f. path. Anat.*, lxx. 139, 1877; lxxviii. 97, 1879; lxxx. 82, 1880), A. Lane (*Guy's Hosp. Rep.*, xlii. 109, 1883–84), R. L. MacDonnell (*Journ. Anat. and Physiol.*, xx. 405, 1885–86), J. H. Scott (*ibid.*, xviii. 339, 1883–84), and others. Sometimes a bifurcation of a costal cartilage occurs (J. Ferrier, *Journ. de méd. de Bordeaux*, xiii. 607, 1883–84). Hunauld seems to have been the first to describe these numerical anomalies in the ribs (*Hist. Acad. roy. d. sc. de Paris, Mém.*, 534, 1744).

A more important, because more evident, costal anomaly is met with in *imperfect development*. In some cases the ribs are simply small in size or flattened or depressed, with the result that the chest-wall loses its normal rounded outline; there may even be a gutter-like depression into which one of the arms appears to fit (Taruffi, *op. cit.*, vii. 162, 1894). Again, some of the ribs may be incomplete, with the result that the osseous framework of the thorax is imperfect. One, two, three, or four of the true ribs with their costal cartilages may fail anteriorly, producing a hiatus in the chest-wall; this defect is usually unilateral, and when it is situated on the left side the heart as well as the lung may be covered only by the soft structures and so be brought more completely within the range of clinical inspection, palpation, and auscultation (T. Smith, *Trans. Path. Soc. Lond.*, xix. 41, 1867–68). There is no constant position in the chest-wall at which these defects are found: they may occur at any level and at any distance from the sternum anteriorly; but, as a rule, the first rib is not affected, the defect is anterior rather than posterior, and the costo-chondral junction is involved. Sometimes the lung protrudes through the opening constituting a pulmonary hernia, as is recorded by E. J. M. Trape (*Thèse*, Bordeaux, 1893), by Sabrazès (*Rev. de méd.*, xiv. 1010, 1894), by J. Schlözer (*Diss. inaug.*, Erlangen, 1842), by C. Seitz (*Arch. f. path. Anat.*, xcviii. 335, 1884), and by H.

Haeckel (*ibid.*, cxiii. 474, 1888). Associated malformations, such as absence or defective development of the pectoral muscles or of the breast and nipple, are not uncommon, and the association is explicable if the teratogenic cause be pressure acting upon an area of the side of the chest; since, also, the hand is often malformed in these cases it is easy to understand how the theory has arisen that constant pressure by the hand in antenatal life might lead to defective development of it and of the part of the chest against which it pressed. To this matter I have already referred (p. 148), but I may again draw the reader's attention to John Thomson's article (with literature list) in *Teratologia*, vol. ii. p. 1, 1895. The cause that presses the hand against the thorax may be amniotic narrowness or bands; in one of my specimens (Fig. 34) the arm was attached to the thorax by a cutaneous band, and there was an extensive defect in the side of the thorax and abdomen, but the defect was apparently much greater than could be accounted for by the manual pressure. The specimen, however, did not agree exactly with those which I have been describing, for in it all the layers of the thoracic wall were wanting and there was an aperture, a more advanced degree of defect than that under discussion at present (*vide* "Pleurosomus," p. 492).

Malformations of the Mammary Glands.

Amazia or absence of the mammary gland is comparatively rare. In 1890 I exhibited to the Edinburgh Obstetrical Society (*Trans.*, xv. 160, 1890) the uterus from a patient who had no mammary glands and no hair on the symphysis pubis; she was twenty-eight years of age, married, but sterile, and her uterus was small in size (1½ inch in length) and malformed (bicornis septus). The vagina, ovaries, and Fallopian tubes appeared to be normal. Defective development of the pelvic organs does not, however, constantly accompany absence of the breasts, for W. Wylie's patient (*Brit. Med. Journ.*, ii. for 1888, p. 235) menstruated regularly and gave birth to a well-formed male child whom she was, of course, unable to suckle, for she had no trace of breasts, areolæ, or nipples. The defect may be bilateral, as in the cases referred to, or, more often, unilateral; generally the nipple is wanting as well as the gland, but sometimes a rudiment of it has been noted (F. Paull, *Lancet*, i. for 1862, p. 648). Incomplete ribs and defective development or absence of the pectoral muscles may occur as associated malformations (King, *Med. Times and Gaz.*, i. for 1858, p. 527). In L. Remfry's patient it was clinically determined that the uterus was absent (*Trans. Obst. Soc. Lond.*, xxxvii. 12, 1896). As may be supposed, the mammary defect usually passes unnoticed till adult life, but it may be detected much earlier if attention happen to be drawn to the chest (J. Thomson, *Teratologia*, ii. 3, 1895); it occurs in males as well as in females; and amniotic pressure suggests itself as a cause, but cannot, of course, be absolutely affirmed.

Hypoplasia of the mammæ (*micromastia*, Taruffi) also occurs; but it is not antenatal but postnatal in its manifestation, becoming apparent, as a rule, at puberty or later. At the same time, the fact that it is often associated with absence of the pectoral muscles (W. Gruber, *Arch. f. path. Anat.*, cvi. 501, 1886), which is undoubtedly antenatal, makes it probable that it also is predisposed to before birth. Further, it may be associated with absence or imperfect formation of the nipple and areola, and with defective development of the uterus and ovaries. Like amazia, its clinical importance begins in adult life when the mammary glands are called upon to perform their normal function.

Athelia or *absence of the nipple* may be met with as the only mammary malformation. In T. Chambers' patient (*Trans. Obstet. Soc. Lond.*, xxi. 257, 1880) the position of the nipples was indicated by a small rose-coloured spot; there were two bodies in the inguinal regions regarded at first as herniated ovaries but afterwards found to be testicles; there was also a rudimentary vaginal canal. Athelia may also occur apart from genital anomalies (W. R. Williams, *Journ. Anat. and Physiol.*, xxv. 304, 1890–91), and it may, of course, be found in micromastia and in amazia.

Polymastia.

Two mammary glands are normally present, but it is not a very uncommon anomaly to find supernumerary mammæ (polymastia) or nipples (polythelia) either in the neighbourhood of the normal glands or in some distant part. This malformation raises several interesting questions and requires a separate paragraph for its description.

Doubtless, polymastia was observed very early in the world's history, and the many-breasted gods and goddesses of the East (*e.g.* the Ephesian Diana) may owe their origin to real instances in human archetypes. Records of actual cases go back to the middle of the sixteenth century; and the literature of polymastia is now very extensive, Taruffi giving seventy-seven references (*Storia della teratologia*, iii. 335, 1886), a number which has recently been greatly augmented.

Supernumerary mammæ occur in males as well as females, and may take the form of polymastia or of polythelia. They have been more often observed in females, possibly because in them attention is specially directed towards the mammary region in connection with lactation. W. F. Adams (*Lancet*, ii. for 1895, p. 462), K. Bardeleben (*Verhandl. d. anat. Gesellsch.*, v. 247, 1891, vi. 199, 1892, vii. 171, 1893; *Anat. Anz.*, vii. 87, 1892), M. Bartels (*Verhandl. d. Berl. Gesellsch. f. Anthrop.*, 201, 1894), E. Evelt (*Arch. f. Anthrop.*, xx. 105, 1891), H. Handford (*Trans. Path. Soc. Lond.*, xxxvii. 568, 1885–86), R. Hilbert, *Memorabilien*, n.F., xii. 129, 1892–93), W. R. Williams (*Trans. Path. Soc. Lond.*, xlii. 224, 1890–91), G. Paravicini (*Arch. di psichiat.*, xxiv. 249, 1903), and F. Griffith (*Med. News*, lxxxii. 21, 1903) have all reported cases of polymastia in the male; P. D. Handyside (*Journ. Anat. and Physiol.*, vii. 56, 1871–73) noted quadruple mammæ in two brothers, and A. Petrone (*Progresso med.*, Napoli, iii. 516, 1889) saw an instance of six mammæ in a male.

In situation, supernumerary breasts show several varieties. Usually they are found on the anterior aspect of the chest below the normal glands and nearer the middle line. Less common situations are the middle line (Percy, *Dict. d. sc. méd.*, Paris, xxxiv. 525, 1819), at a point external to the mammillary line (Charcot and Le Gendre, *Compt. rend. Soc. de biol.* 3 s., i. 164, 1860), a point above and outside the mammary region (P. Shannon, *Dublin Quart. Journ. Med. Sc.*, v. 266, 1848), or over the acromion process (Klob, *Ztschr. d. k. k. Gesellsch. d. Aerzte zu Wien*, xiv. 815, 1858). In February 1895 I saw a case of supernumerary mamma (without a nipple) in the right axilla of a primipara in the Edinburgh Maternity Hospital (under Dr. Berry Hart's care); the gland gave rise to some trouble during the puerperium and was thus discovered. The axilla and the anterior axillary border are among the more common situations (N. Perreymond, *Union méd.*, ii. 864, 1874; M. Notta, *Arch. d. tocol.*, ix. 108, 1882; A. Neve, *Lancet*, i. for 1894, p. 801; E. Martin, *Ann. d'ocul. et gynéc.*, i. 185, 1838; Lichtenstern, *Arch. f. path. Anat.*, lxxiii. 222, 1878; etc.). Supernumerary mammæ also occur outside the limits of the thorax, and although they do not then strictly fall to be considered in this chapter, I may briefly refer to them. They have been found, for instance, upon the back, as C. F. Paullinus records ("Mammæ in tergo," *Miscell. Acad. nat. curios.*, Dec. ii., Ann. iv., Appendix, p. 203, 1686), on the thigh (Chaussier and Magendie, *Journ. de physiol. expér.*, vii. 175, 1827; L. Testut, *Bull. Soc. d'anthrop. de Paris*, 4 s., ii. 757, 1891; C. D. Homans, *Boston Med. and Surg. Journ.*, lxxiv. 181, 1866), in the vulvar labia (E. Hartung, *Diss. inaug.*, Erlangen, 1875), on the cheek (A. Barth, *Arch. f. path. Anat.*, cxii. 569, 1888), on the upper part of the anterior abdominal wall (*Centralbl. f. Gynäk.*, x. 730, 1886), and within ovarian dermoids (Bland-Sutton, *Ovaries and Fallopian Tubes*, 58, 1891; *Tumours*, 405, 1903). Supernumerary mammæ in the anterior abdominal wall below the level of the umbilicus are apparently very rare; Windle, however, in his eleventh report on recent teratological literature, refers to a case (in a man), apparently well established, reported in 1899 by Braquehaye, in which there was an accessory gland midway between the navel and the penis; T. J. M'Gillicuddy (*Med. Rec.*, New York, xl. 446, 1891) described another case, also in a man, where there were two mammæ, one on each side of the umbilicus.

As a general rule there is only one accessory breast, and when this is the case it is usually on the left side (Lichtenstern); there may, however, be two, and then they are commonly but not invariably symmetrical; three have been observed (Percy, *Journ. d. méd. chir. pharm.*, ix. 378, 1805); and Neugebauer some years ago sent me the photograph of a woman having the large number of eight (*Centralbl. f. Gynäk.*, x. 729, 1886). The latter case, however, is rather an instance of multiple nipples (polythelia) than of supernumerary mammæ. R. E. Fitzgibbon saw a man who had four accessory nipples (*Dublin Quart. Journ. Med. Sc.*, xxix. 109, 1860).

In many cases the accessory gland has a distinct nipple and areola, but these may both be absent; on the other hand, the nipple or the areola may be the only representative of the breast that is found. At the present time (June 1904) I have under my care a pregnant woman with an accessory areola under the left one; it has become darker during pregnancy and distinctly shows little spots like Montgomery's follicles; it is about one-third the size of the normal areola. The supernumerary mamma is generally much smaller than the normal one, and is sometimes connected with it by a canal of communication.

I have not here to deal with the postnatal history of polymastia, but it may be said that sometimes such accessory glands become functionally active during lactation, and secrete milk which can be drawn off through the nipple. In other cases the milk exudes through a sinus which takes the place of the mammilla, and in others it is retained, setting up a painful swelling of the breast and leading to the formation of an abscess. Accessory breasts are not exempt from cancer (F. T. Paul, *Brit. Med. Journ.*, ii. for 1894, p. 1309).

Associated malformations seem to be rare in polymastia, a teratological fact which no doubt has a meaning if it could be discovered. J. P. Prückel (*Miscell. Acad. nat. curios.*, Dec. i., Ann. ix. et x., obs. viii., p. 45, 1680) describes very briefly a case of polythelia accompanied by polydactyly (six digits on each extremity); and Anne Boleyn, one of the wives of Henry VIII., is said to have been deformed in the same way.

The Comparative Teratology of polymastia, as might be expected, is full of interest, and of interest which has not yet been exhausted by research. Since mammary glands are confined to the mammalia, it is only in these animals that their anomalies come under consideration. When there are normally many mammæ in an animal they are usually arranged in two parallel rows along the ventral aspect of the body; and when they are less numerous either the abdominal or the thoracic members of the series may be absent; in man and the monkeys, for instance, it is supposed that the inguinal mammæ have aborted leaving only the pectoral pair. In the lemurs almost all the possible mammary arrangements may be noted in the different species. J. Bland-Sutton (*Evolution and Disease*, 162, 1890) gives an interesting account of this subject, and records two cases of polymastia in monkeys, and refers to instances in the cow, the goat, the sheep, and the female zebu.

From the comparative teratology of polymastia we pass naturally to its teratogenesis, for the most widely accepted view is to regard it as an atavistic phenomenon, a reversion to an original type possessing more than two mammary glands. When additional mammæ or nipples occur on the thorax or abdomen along the lines of the deep and superior epigastric arteries, the atavistic theory has strong claims upon our belief, and it seems reasonable to regard them as representing the mammary glands of other mammals. The occurrence, however, of erratic mammæ, their presence, for instance, in the axilla, on the thigh, or over the acromion process, introduces difficulty and doubt into the question. These can hardly be looked upon as atavistic, and Darwin himself admitted this. Ahlfeld's theory of transplantation of surface tissues to other parts of the body by amniotic pressure scarcely commends itself as a reasonable explanation (*Die Missbildungen des*

Menschen, p. 110, 1880). The view which seems best supported at the present time is to look, with Bland-Sutton, upon polymastia as explicable in some cases by atavistic reversion, in others by dichotomy of a single gland (as when there are bifid nipples), and in others as a spontaneous variation or sport. When, however, we come to look more closely into the embryological aspect of the matter we get, as we nearly always do, some fresh light upon the subject. H. Schmidt (*Anat. Anz.*, xi. 702, 1896), being struck by O. Schultze's discovery of a milk line or ridge in embryo pigs (*Sitzungsb. d. phys.-med. Gesellsch. zu Würzburg*, 77, 1892), made careful observations regarding its possible presence in the human subject. At first his researches gave negative results, but later (*Morphol. Arb.*, vii. 157, 1897) he found in human embryos of about 15 mm. long a line of elevated epithelium on the side of the thorax and abdomen; this he termed the "milk streak." Within or along this streak were the *anlagen* of the normal mammæ, but in longer embryos (26 to 60 mm.) there were also epithelial *anlagen* of various sizes and positions, which he regarded as the earliest stages of supernumerary milk glands; they occurred in the axillæ, on the anterior and lateral walls of the thorax, and in the inguinal region, the positions where hyperthelia and hypermastia (polymastia) most often are seen in the adult. There is, therefore, no necessity to invoke atavism or dichotomy or "sport," for there are in the embryo rudimentary mammæ, and it is sufficient to say that here as in other malformations an arrest of development serves to account for the anomaly. Instead of entirely disappearing, as is normal, one or more of the supernumerary *anlagen* remain and give rise to polymastia and polythelia. Dauthuile (*Thèse*, Lyon, 1899) holds similar views and meets the difficulty of explaining the erratic mammæ of the back, thigh, and face, by insisting upon the close histological relationship between mammary and sebaceous tissues; pseudo-mammæ may originate from sebaceous glands in any part of the body. It seems safe, therefore, to conclude that when supernumerary breasts or nipples develop in the "milk streak" they represent the persistency of structures which ought to be transitory, and that when they occur elsewhere they are not real mammæ but giant sebaceous glands. Bland-Sutton's observation upon the tendency of protected cutaneous surfaces (*e.g.* the skin in the axilla) to become glandular may be held as supporting this view of the origin of pseudo-mammæ outside the "milk streak." The fact that polymastia is not infrequently hereditary (Tiedemann, *Ztschr. f. Physiol.*, v. 110, 1835; Pétrequin, *Gaz. méd. de Paris*, v. 197, 1837; J. C. Saunois, *Thèse*, Paris, 1812; Garland, *Edinb. Med. Journ.*, xxiii. 45, 1877–78) does not form an argument against the theory of arrested disappearance of primitive *anlagen*, for heredity exists in many anomalies which are capable of this explanation. It simply suggests the presence of a germinal factor which in some way leads to the persistence of states which are normally transitory.

Muscular Anomalies of the Thorax.

Absence or imperfect development of the *pectoral muscles* is one of the most characteristic of the muscular anomalies of the thorax. It has already been alluded to in connection with costal and mammary defects, and requires only a short notice here. John Thomson's article (*Teratologia*, ii. 1, 1895), besides containing records of three cases, brought together a wealth of information on the subject of this anomaly; and although many papers have appeared since its publication, they have not altered appreciably the conclusions contained in it.

Both the pectoralis major and minor may be absent or defective, and yet, as was noted also in connection with absence of the clavicles, there may be very little consequent inconvenience. The power of using the arm may not be appreciably diminished (H. M. Bowman, *St. Barth. Hosp. Rep.*, xxx. 125, 1894), and, as a matter of fact, the muscular anomaly may be discovered accidentally, as in the examination of recruits. At the same time the appearance of the chest is characteristic. There is a marked depression in the pectoral region on one or both sides; when it is unilateral, the one side of the chest is flatter and has smaller measurements than the other; the mammary gland and nipple may be absent or poorly developed; it was frequently noted that a fibrous band (patagium) passed from the ribs to the humerus; and several neighbouring muscles have in certain instances been found to be defective (*e.g.* serratus magnus, latissimus dorsi, intercostals, teres major and minor, etc.). When the pectorals were only defective and not entirely absent, it was generally the lower or sterno-costal part that showed the anomaly. The right side was apparently more often the seat of this deformity than the left, and males were five times as often affected as females (Thomson, *loc. cit.*). In some cases in adults the axillary and mammary hair (M. Schein, *Arch. f. Dermat. u. Syph.*, lxviii. 323, 1904) was observed to be absent, there was very little subcutaneous fat in the chest-wall, and the skin occasionally showed a congenital scar. Other associated malformations were absence of parts of the ribs and sternum (*q.v.* p. 470), and of the hand and arm (*e.g.* syndactyly, absence or shortness of digits, curving of the forearm, etc.). It is possible that both the pectoral defect and the associated malformations may be due to prolonged pressure of the arm against the chest in antenatal life; this may, in its turn, be caused by narrowness of the amnion. Heredity seems to be very seldom associated with this anomaly.

Thomson gives the literature of the subject up to 1894; the following later references may be added:—Cruchet, *Journ. de méd. de Bordeaux*, xxv. 569, 1895; B. Prinz, *Diss. inaug.*, Würzburg, 1894; Overweg, *Deutsche mil.-ärztl. Ztschr.*, xxiv. 440, 1895; Hofmann, *Arch. f. path. Anat.*, cxlvi. 163, 1896; Joachimsthal, *Berl. klin. Wchnschr.*, xxxiii. 804, 1896; M. Kaiser, *Ztschr. f. klin. Med.*, xxxii. Supplhft., 174, 1897; H. Morestin, *Bull. Soc. anat. de Paris*, 5 s., x.

144, 1896; J. Azam et J. Casteret, *Presse méd.*, 53, 1897; J. Hutchinson, *Arch. Surg.*, viii. 355, 1897; A. Schmidt, *Deutsche Ztschr. f. Nervenh.*, x. 400, 1897; G. A. Sutherland, *Clin. Journ.*, xi. 173, 1897–98; Fallot, *Marseille méd.*, xxxv. 54, 1898; E. W. Schneller, *Med. Rec.*, liii. 282, 1898; J. Harold, *Lancet*, i. for 1898, p. 499; M. Lengsfelden, *Wien. klin. Wchnschr.*, xv. 1306, 1902; W. R. Williams, *Lancet*, i. for 1903, p. 613; J. Martirené, *Rev. d'orthop.*, 2 s., iv. 209, 1903; Bötticher, *Deutsche med. Wchnschr.*, xxix. Ver.-Beil., 158, 1903; Grisel, *Rev. d'orthop.*, 2 s., iv. 359, 1903; D. Zeiliger, *Prakt. Vrach*, ii. 611, 635, 1903; H. W. Smith, *Amer. Med.*, vi. 734, 1903; L. A. Harriehausen, *Diss. inaug.*, Göttingen, 1903; and E. Joüon, *Rev. d'orthop.*, 2 s., v. 71, 1904.

Other muscular anomalies of the thorax are found in the presence of a *musculus sternalis* or *presternalis*, as has been noted in connection with anencephaly (*q.v.* p. 347), and regarding which various writers have stated their views (Samiac, *Toulouse méd.*, 2 s., v. 99, 1903; Halipré et Cauchois, *Normandie méd.*, xviii. 453, 1903; Piollet, *Lyon méd.*, ci. 832, 1903); other supernumerary muscles are considered by G. S. Huntington (*Proc. Assoc. Amer. Anat.*, p. xii. 1902–03). Absence of the *trapezius* has been described by A. Schüller (*Wien. klin. Wchnschr.*, xvi. 516, 1903) and by H. von Haffner (*Internat. Monatschr. f. Anat. u. Physiol.*, xx. 313, 1903), and of the *deltoid* by Fortin and Chaplain (*Normandie méd.*, xviii. 299, 1903). Without doubt, however, the most important muscular anomaly in connection with the thorax is defect of the diaphragm leading to congenital diaphragmatic hernia: that subject requires several paragraphs to itself.

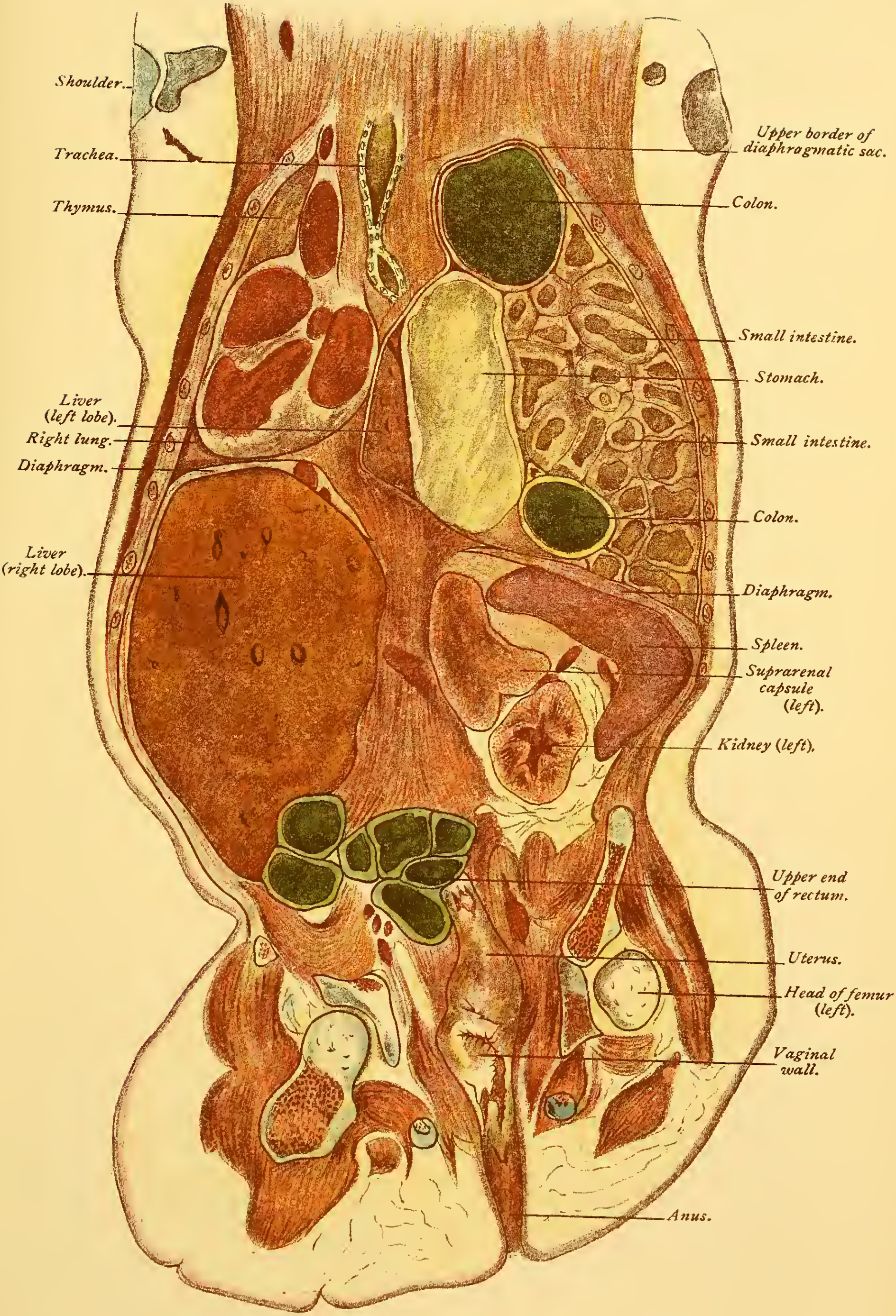
Congenital Diaphragmatic Hernia.

Congenital diaphragmatic hernia is a grave malformation unaccompanied by any external sign of its existence. It is essentially an anomaly in the relations of the abdominal to the thoracic viscera, and as such gives no indication of its presence until either the abdomen or the thorax is opened into. It is a comparatively common malformation, as is demonstrated by the fact that I have been able to collect from medical literature no less than a hundred cases published between the years 1888 and 1900. Many cases had been reported prior to 1888, and there have been others since 1900, so that it may be concluded that the bibliography is a large one. There were three personal observations in my list of a hundred cases: one (Plate XXIII.) was an infant externally normal in appearance; another (Fig. 74) was an anencephalic fœtus; and the third was an iniencephalic fœtus (Plate XVI.). I shall describe in detail the first of these three specimens (Plate XXIII.), for it will serve to set forth the typical characters of the anomaly in a striking fashion.

The infant, a full-time female, was born without instrumental aid. The confinement took place in the outdoor department of the Edinburgh Medical Mission Dispensary, in January 1896. The presentation was the vertex, and the child was large, well formed externally, and apparently healthy. She was stillborn however, and although efforts at breathing were made, and although attempts at resuscitation were continued for a long time, respiration was never fully established. The parents were said to be healthy. Dr. Graham, the Resident at the Dispensary, began to make an autopsy in the usual manner; but on opening into the thoracic cavity he found some coils of intestine; so, diagnosing a grave malformation, he replaced the chest-wall and communicated with me. I decided to make a coronal frozen section of the body, and in this manner to make clear the displacement of parts which was evidently present.

The trunk was frozen the usual way, and a vertical coronal section was made, which passed through the shoulder joints above and the hip joints below. I had hoped that the section would have included the defective part of the diaphragm (for I had made up my mind that such an anomaly existed), but unfortunately it passed just posterior to the defect which was afterwards found to occupy the portion of the diaphragm which normally comes into relation with the pericardial sac; in the lower part of the trunk, also, it passed between the uterus and bladder, showing neither well. The most striking appearance seen on section was the presence of a large number of the abdominal organs in the left half of the thoracic cavity.

The posterior slab of the section (Plate XXIII.) showed very plainly the misplacement of the abdominal and thoracic viscera; unfortunately, it passed, as has been said, behind the herniated part of the diaphragm. It, therefore, showed no break in the continuity of the diaphragm, either on the right side or on the left; but it was clear from it that the left side of the thoracic cavity contained a sac, afterwards found to be made up of thinned-out diaphragm, which contained small intestines, stomach, and colon. In the right side of the thorax was the heart in the pericardial sac, and above it was the thymus gland. When the heart was lifted up, the right lung, consisting of three lobes and quite unexpanded, was found lying behind it. In the middle line the trachea was seen twice cut into in this section; it was displaced towards the right side. Immediately to the right of the distended stomach was a part of a gland which further investigation showed to be a piece of the left lobe of the liver. It was thought at first that the left lung was absent; but a prolonged search revealed it, small in size (1 inch in diameter), lying in the apex of the thoracic cavity, a little to the left of the middle line, and in close contact with the upper loop of colon, but separated from it by the diaphragmatic sac. Below the diaphragm on the left side was the spleen in section, measuring about 1¾ inch by 1 inch. Below and internal to it was the left kidney and suprarenal capsule, while in the middle line were the soft structures in front of the vertebral column. On the right side was the right lobe of the liver, measuring, as seen in this section, about 2½ inches vertically and 2 inches transversely. Below the liver was a loop of large intestine, containing meconium, which was found, on further examination, to be the commencement of the sigmoid flexure; below


Shoulder.
Trachea.
Thymus.
Liver (left lobe).
Right lung.
Diaphragm.
Liver (right lobe).
Upper border of diaphragmatic sac.
Colon.
Small intestine.
Stomach.
Small intestine.
Colon.
Diaphragm.
Spleen.
Suprarenal capsule (left).
Kidney (left).
Upper end of rectum.
Uterus.
Head of femur (left).
Vaginal wall.
Anus.

it, and nearer to the middle line, was another piece of large intestine, the upper part of the rectum. Still lower down was the uterus, and below it was the vagina cut into in two places. Quite at the lower border of the slab, the anal canal had been opened into. The right kidney and suprarenal capsule, lying behind the right lobe of the liver, were seen only when it was raised.

A study of the anterior slab of the section brought out several additional particulars. On the right side of the middle line the thorax was seen to contain the heart, the thymus gland, part of the left lobe of the liver, and the left lung; on the left side were the small intestines, the distended stomach, and the loop of colon. Immediately anterior to the parts seen in this section was the defect in the diaphragm, which consisted of a membranous sac extending up into the thoracic cavity, into which could be seen passing the loop of colon (found to be the transverse) and the coils of small intestine. The loop of meconium-containing bowel in the upper part of the thorax turned out to be the cæcum with appendix vermiformis attached to it. Below the diaphragm were seen the same parts as in the posterior slab, with, in addition, coils of small intestine in the middle line, and below them the sigmoid flexure and urinary bladder. In the lowest part was the vaginal canal, for the section had passed between the bladder and uterus, just shaving off a bit of the cervix uteri. The tube and ovary of the right side were seen just above the upper end of the bladder.

From the comparison of the two slabs of the frozen section it was possible for me (with a little extra dissection) to arrive at a conclusion regarding the nature of the malformation from which this infant was suffering, and which had proved fatal to her postnatal life, although it had in no way interfered with her antenatal existence. The anterior part of the left side of the diaphragm was deficient in muscular tissue, and projected upwards as a membranous sac, filling the whole of the left side of the thorax. In this sac were the small intestines (ileum chiefly), the stomach, the transverse and ascending colon, and the greater portion of the left lobe of the liver. Above the sac was the undeveloped left lung. Through this intrusion into the left side of the thorax of the structures which normally occupy the abdomen, the heart was displaced to the right, and the thymus gland with it, while the development of the left lung was practically stopped. During its displacement the heart seems to have been rotated, for the left ventricle lay anterior and the right behind. It seemed also that the drag of the dislocated abdominal viscera on the left side had brought the corresponding kidney and suprarenal capsule forward.

Since the herniated abdominal viscera were contained in a distinct membranous sac, this case fell to be classed as one of *hernia diaphragmatica vera*, or true diaphragmatic hernia, of the left side, situated in the space between the portio sternalis and the portio costalis of the diaphragm. But the presence of the sac is not a constant character, and I have met with a case in which it was absent, constituting *hernia diaphragmatica spuria*. This was in an anencephalic fœtus, sent to me for examination by Dr. Millard. It was a female, and its birth was preceded by a pregnancy characterised by excessive vomiting. The gestation had just passed the seventh month when labour occurred; there was marked hydramnios, the quantity of liquor amnii (of a turbid brown colour) being estimated at 2½ gallons. Forceps had to be used to extract the fœtus. The placenta was entirely adherent, and had to be picked off with the fingers; it was very large, but also very thin, in no part being more than ½ inch in thickness, and generally being ¼ inch; there were two or three fatty patches in it. The mother was thirty-nine years of age, and had had one previous labour, ending in the birth of a dead infant. She came of a healthy family, and was herself healthy and well developed, but very nervous. The fœtus was frozen for examination, and, since I had no suspicion that the internal organs presented any anomalies other than those usually found in anencephaly, I made the customary mesial sagittal section. The right side of the section is shown in Fig. 74.

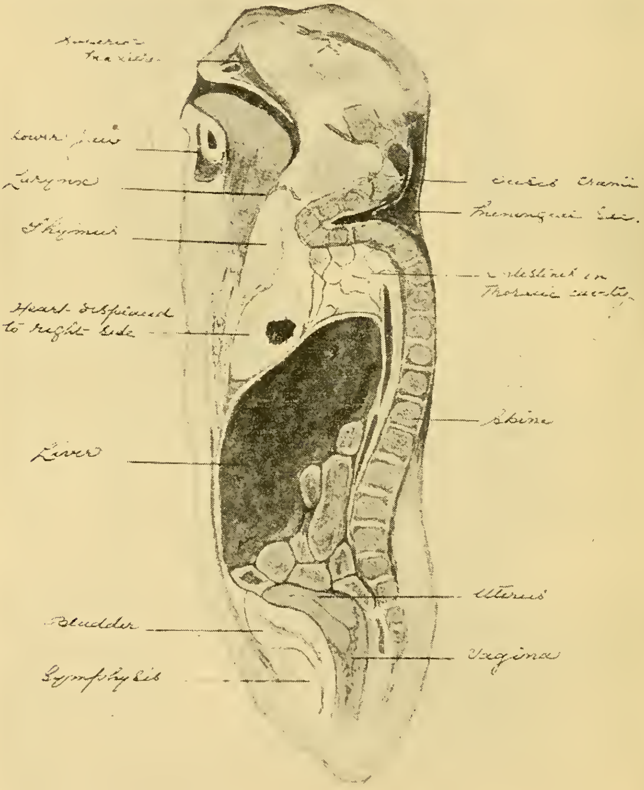


FIG. 74.—Congenital Diaphragmatic Hernia in an Anencephalic Fœtus. Sectional appearances. Specimen No. 204.

The section showed very clearly the defect of the cranial bones, the backward direction of the basis cranii, the extraordinary bending of the vertebral column in the cervical and upper dorsal regions, and the condition of spina bifida affecting nearly the whole length of the spine. In addition, however, to these changes, which are practically common to all cases of anencephaly, the section showed also that the internal organs did not bear a normal relation to each other. The heart lay entirely to the right of the middle line of the body; for the vertical sagittal section had passed between it and the pericardium, leaving the latter in the left slab of the section. The thorax, behind the heart, contained coils of small intestine, while to the front was situated the thymus gland. When the heart was lifted up and the pericardial sac cut through, it was found that the right lung was lying quite unexpanded in the right side of the thorax. The diaphragm on the right side was quite normal, and below it lay the right lobe of the liver. Below it again were some coils of small intestine and the commencement of the sigmoid flexure, and lying partly above and partly below the pelvic brim were the urinary bladder and uterus, the latter in a position of marked anteversion. When the left slab of the section was examined the following additional particulars were made evident. There was no diaphragm at all on the left side, and the abdominal organs simply passed up into the left side of the thoracic cavity as if it were a part of the abdomen. Consequently, above the level of the place where the diaphragm ought to have been there were found the left lobe of the liver (somewhat deformed), part of what was probably the transverse and descending colon, the stomach (in a contracted condition), and several coils of small intestine. Quite in the apex of the left side of the thoracic cavity was a small lung, the left, in an almost undeveloped state; it was not separated from the coils of intestine by a membranous sac, and in this respect the arrangement differed from that in the preceding case where there was not actual absence of the diaphragm but only the projection of a non-muscular extension of it into the thoracic cavity. I could find no trace of the spleen. In the lower part of the abdominal cavity on the left side were coils of small intestine and the cæcum and appendix vermiformis, along with a portion of the ascending colon. The kidneys occupied their usual position, one on each side of the vertebral column. Only twenty vertebræ could be counted in the spine, the absent members being apparently chiefly dorsal.

In the second specimen, therefore, there existed that form of diaphragmatic hernia to which the name *spurious* or *false* has been applied; for the diaphragm showed a complete unilateral defect, and the displaced abdominal viscera had consequently no sac. A somewhat similar specimen was examined by me in 1899. It has been described on page 279, and is figured in Plate XVI.; it was an instance of iniencephaly, and, as in the former cases, the existence of a diaphragmatic defect was not suspected till a section was made.

From the description of these specimens the reader will have obtained some idea of the clinical features and morbid anatomy of congenital diaphragmatic hernia; but I may add here some further details on both these matters, making use of my unpublished analysis of one hundred cases reported in various parts of the world between 1888 and 1900. I append (on p. 486) the literature list and refer to the cases simply by numbers.

It is a striking fact that little or nothing is stated regarding the health of the mother in most of the one hundred cases of fœtal diaphragmatic hernia. In one instance (18) she had syphilis; in another (76) she had mitral disease; but in all the other cases there is nothing to lead us to think that the mother was an unhealthy woman before she became pregnant with the fœtus which showed this deformity. In no case is there the record of family prevalence of the diaphragmatic defect or of heredity. In only twenty-three cases are we told the parity of the mother: she was a primipara in five (18, 34, 51, 55, 82), a secundipara in seven (6, 42, 67, 83, 85, 88, 98), a quadripara in two (68, 96), a quintipara in two (75, 76), a sexipara in two (90, 100), an octipara in one (81), a nonipara in one (99), and a "multipara" in three (1, 8, 49). In no less than seventy-five cases no information was forthcoming regarding the symptomatology of the pregnancy: in twelve out of the twenty-five cases in which some facts were supplied to us the pregnancy went to the full term, and, in the remaining thirteen, labour occurred more or less prematurely. In five instances the gestation was complicated by hydramnios (49, 67, 68, 98, 100), in one by dispnœa (76); in one the pregnancy was plural (40), and in one the product was a double-headed monster (49). By far the most interesting pregnancy-history was that furnished by J. Ikeda of Fukuoka, Japan (30): it was the case of Ikeda's wife. She noticed that at the beginning of the eighth month of her pregnancy rhythmic movements of the fœtus began to be felt, and were most marked to the left of the umbilicus. Ikeda made an examination at the time, and made out that the fœtus was lying L.O.A., and that the fœtal heart-rate was 152 per minute. He also felt quite distinctly the peculiar fœtal movements: they occurred several times in the twenty-four hours, consisted of from ten to twenty taps, and lasted from ten to fifteen minutes with pauses of a few seconds. They were regarded by Ikeda and his wife as hiccough or singultus of the fœtus, a conclusion which was borne out by the postnatal history of the infant; at the autopsy, the infant having died when eight days old, a diaphragmatic hernia was found.

In seventy out of the hundred cases no facts regarding the labour were stated; in eighteen it was described as normal; in the remaining twelve it was prolonged, preternatural, or complex, but even in them it is probable that it was not the diaphragmatic hernia but associated morbid states (hydramnios, placenta prævia, adherent placenta) that led to the disturbance of labour. It is unlikely that such a concealed malformation as hernia of the diaphragm should have any effect on the progress of the confinement.

The clinical history of the infant was generally stated, and was strikingly similar and brief. Thus, in fifty-three out of the hundred cases, the child was stillborn, or gave only a few gasps, dying within one hour. In a few cases, however, life lasted for a short time: for two hours (40), three and a half hours (43), six hours (36), twenty-four hours (34, 66, 69), forty-three hours (44), fifty-five hours (99), two days (39), seven days (57), eight days (30), two and a half months (74), five months (84), and fourteen months (88).

In quite another group of cases the diaphragmatic hernia, although congenital, was only discovered some years after birth, *e.g.*, at the age of three and a half years (5), of eight (71), of sixteen (14, 73), of nineteen (9), of twenty-two (52), of twenty-four (7), and of twenty-seven (20). In some remarkable cases it was only recognised at an advanced age, *e.g.*, at fifty years (29, 78), at fifty-five (86), at fifty-seven (50), and at sixty-seven (53). It is evident, therefore, that in some of its forms congenital diaphragmatic hernia does not interfere with postnatal life.

The male sex seems to be more liable to hernia of the diaphragm than the female; thus in the hundred case-records collected by me there were forty-seven males and twenty females, and in the remaining thirty-three instances the sex was not stated. In nine cases (1, 2, 24, 30, 41, 42, 56, 58, 90) it was noticed by the medical attendant that the heart was pulsating on the right side of the chest at birth; in one case (68) the presence of epigastric depression was observed; but neither in the new-born infant nor in the adult was the diagnosis of diaphragmatic hernia often made during the life of the subject.

An interesting clinical history was furnished by J. O'Dwyer (5). The patient was a boy, three and a half years of age, who had been sick for four days. He had severe dyspnœa and prostration; his temperature was 105° F.; and there had been obstruction for two days. There was flatness over the posterior part of the left side of the chest with absence of respiratory sounds, and a moderate dulness anteriorly with broncho-vesicular breathing at the upper part. There was resonance of a somewhat tympanitic quality in the sixth interspace in the axillary line. The heart was displaced to the right, with the apex beat in the epigastrium. The case was diagnosed as one of empyema, and a needle was inserted, but with no result. Eight days later the bowels were freely moved with cathartics, and the temperature became normal but the general condition remained poor. Several attacks similar to the above were recorded during the following two months. In the last of these no relief followed evacuation of the bowels with cathartics. The left side of the chest measured ¾ inch more than the right. O'Dwyer diagnosed empyema with positiveness; but the insertion of a large needle and then of a trocar brought no pus. A large opening was then made in the sixth intercostal space, and *intestine appeared*; the wound was closed. On the following day another opening was made into the pleural sac lower down (tenth interspace), and an opening in the muscular part of the diaphragm (1½ inch in diameter) was found. About 3 inches of the ninth and tenth ribs were removed, and the floating ribs were drawn down, and so O'Dwyer got room to insert his whole hand. He had some difficulty in replacing the intestines in the abdominal cavity, the cæcum being the last part to be reduced. The edges of the wound were then pared and strong braided silk sutures passed; even after being sutured, the diaphragm bulged greatly into the pleural cavity. Death occurred six hours later.

Want of space forbids the citing of other instances of the postnatal clinical history of cases of diaphragmatic hernia; but O'Dwyer's patient may be taken as typical of the cases in which the child survives its birth, although there are many variations in the symptomatology according to the mode in which the abdominal organs are displaced into the thoracic cavity.

A great deal has been written regarding the *morbid anatomy* of congenital diaphragmatic hernia. The cases which I have described will have given the reader an idea of the two outstanding varieties, the form with a sac and that without one, the true and the spurious as they have been called; but some additional facts may be stated. The sac of the true hernia consists of parietal peritoneum and of a greater or smaller part of the parietal pleura, and sometimes some fibres of the centrum tendineum of the diaphragm are found in the wall. The hernia may be on the left side and may take place through an opening between the portio sternalis and the portio costalis of the diaphragm, or through or in the neighbourhood of the foramen œsophageum, or in the middle of the left half of the tendinous part of the diaphragm, or posteriorly somewhere in its circumference. On the other hand, the opening may be on the right side (Lepage, *Compt. rend. Soc. d'obst., gynéc., paed. de Paris*, v. 160, 1903) in situations corresponding to the above (with the exception of that through the œsophageal aperture). Again, there may be not so much a hernia as a dome-shaped distension of the diaphragm upwards—eventratio diaphragmatica (Arnheim, 59); this is rare, and has only been seen on the left side; the wall consists of peritoneum, of pleura, and of the greatly distended and thinned-out tendinous and muscular part of the diaphragm. In the spurious form of diaphragmatic hernia there is, as has been stated already, no sac. The abdominal contents simply occupy the pleural cavity. There are several varieties: the whole diaphragm may be absent; the left half may be entirely wanting, or there may be a large opening in it, or there may be smaller openings (*e.g.* through foramen œsophageum, between the sternal and costal part, in the centrum tendineum, between the pars lumbalis et costalis, at the entrance of the sympathetic nerves); the right half may be entirely wanting, or may show a large defect, or may exhibit smaller openings (*e.g.* in centrum tendineum, between the pars lumbalis et costalis, posteriorly near the vertebral column, etc.). With regard to the viscera which may be displaced, all kinds of varieties and associations may be met with: all the abdominal viscera including the kidneys and suprarenal capsules may be found in the thorax; on the other hand, only a small part of the stomach or liver may be found therein; and all the intermediate types may be noted. The displaced organs, especially the liver, may show deformities; the lungs are always small and poorly developed; and the heart generally lies much to the opposite side.

Associated malformations have been noted: non-descent of testicles

(6, 28, 65), absence of ulna and presence of a uterus unicornis cum cornu rudimentario (42), diprosopus triophthalmus (49), facial hemiatrophy (55), double uterus and vagina (55), hare-lip and cleft palate and congenital teeth (81), interventricular opening in heart (81), congenital goitre (96), iniencephaly (100). There were multiple malformations in P. Nau's case (*Bull. et mém. Soc. anat. de Paris*, lxxviii. 594, 1903). Anencephaly, also, would appear to be sometimes associated with diaphragmatic hernia; for, in addition to my specimen (98), cases have been reported by Otto (*Monstrorum sexcentorum descriptio*, Nos. 38 and 44, pp. 24, 28, 1841), by Gruber (*Arch. f. path. Anat.*, xlviii. 391, 1869), and by Bischoff (*Arch. f. Gynæk.*, xxv. 445, 1885).

The *teratogenesis* of congenital diaphragmatic hernia does not present many difficulties, and if the details of the development of the diaphragm were fully and accurately known, even these would doubtless be capable of explanation. Obviously, non-development of the great muscular partition between the thorax and abdomen accounts for the cases of spurious hernia in which there is no sac for the dislocated abdominal viscera; defective development of muscular fibres in the diaphragm may explain the cases of hernia diaphragmatic vera. So much is clear, but when we come to inquire into the reasons why lateral defects are more common than mesial, and why the left side is more often affected than the right, difficulties arise. In birds, for instance, the diaphragm consists of two lateral parts not connected together in the middle line, and it has therefore been thought that in mammals the mesial portion of the diaphragm has been superadded; if such be the case, then, according to the theories of evolution and degeneration, the mesial part ought to be that which is most frequently absent. Teratology, however, would seem to show that the mesial part is the first formed, for it persists when the lateral parts are wanting. The explanation of this and other difficulties doubtless lies in the ontogenesis of the diaphragm, and in time we shall know all the stages of this somewhat obscure part of development. Already Franklin P. Mall's article (*Johns Hopkins Hosp. Bull.*, xii. 158, 1901) has done something to clear up disputed points. One fact the teratologist must bear in mind in thinking over the origin of malformations of the diaphragm, namely, that structures which are internal in the fully-formed embryo are often external in the early stages, and so come under the influence of teratogenic causes external to the organism. At the same time it must be freely admitted that the cause of the defect in the diaphragm is very obscure: it may be traction upon the vitelline or umbilical duct; primary shortness of the œsophagus may be a starting-point (E. Rabaud, *Bull. Soc. d'obst. de Paris*, vi. 352, 1903); or the presence of a common mesentery for the large and small intestine may, by permitting greater freedom of movement to the bowel, predispose to it. The matter is well worthy of further investigation, and the articles of Otto Grosser (89) and of E. Schwalbe (91) will prove of service in indicating the lines along which research may most usefully advance; Liepmann (*Arch. f. Gynæk.*, lxviii. 780, 1903) also gives a good summary of recent views.

Literature.—In addition to the one hundred cases, references to which appear below, the reader may be directed to the articles of H. I. Bowditch (*Buffalo Med. Journ.*, ix. 1, 65, 1853–54), of L. Lacher (*Deutsches Arch. f. klin. Med.*, xxvii. 268, 1880–81), and of A. Boursier (*Dict. encycl. d. sc. méd.*, 1 s., xxix. 1, 1884) which contain literature lists; many references are also given in the *Index Catalogue* of Washington, 1 s., vol. vi. 154, 1885; 2 s., vol. vii. 15, 1902, under the heading, "Hernia, Diaphragmatic." (1) Korn, *Centrlbl. f. Gynäk.*, xii. 523, 1888. (2) A. M. Paterson, *Brit. Med. Journ.*, ii. for 1888, p. 1207. (3) Fleischmann, *Centrlbl. f. Gynäk.*, xiii. 79, 1889. (4) C. Liman, *Handbuch d. gerichtlichen Medizin*, Bd. ii. p. 11, 1889. (4*a*) A. Monnier, *Thèse*, Paris, 1889. (5) J. O'Dwyer, *Arch. Pediat.*, vi. 882, 1889. (6) G. Schröter, *Diss. inaug.*, Königsberg, 1889. (7) N. Fried, *Internat. klin. Rundschau*, iv. 522, 1890. (8) O. Schaeffer, *München. med. Wchnschr.*, xxxvii. 536, 1890. (9) W. Turner, *Lancet*, i. for 1890, 1301. (10) Dehn, *München. med. Wchnschr.*, xxxviii. 227, 1891, Three cases. (13) O. H. J. Frantz, *Diss. inaug.*, Kiel, 1891. (14) W. A. Hollis, *Lancet*, i. for 1891, p. 1095. (15) J. Kaup, *Diss. inaug.*, Kiel, 1891, Two cases. (17) A. Larsen, *Hosp.-Tid.*, 3 R., ix. 287, 1891. (18) O. J. Mayer, *Diss. inaug.*, Berlin, 1891. (19) Sir J. Paget, *Studies of Old Case-Books*, p. 149, 1891. (20) C. Reinhard, *Deutsche med. Wchnschr.*, xvii. 954, 1891. (21) H. R. Spencer, *Trans. Obst. Soc. Lond.*, xxxii. 132, 1891, Three cases. (24) G. N. Pitt, *Trans. Path. Soc. Lond.*, xliii. 79, 1891–92. (25) Niemöller, *Berl. klin. Wchnschr.*, xxix. 355, 1892. (26) H. R. Spencer, *Trans. Obst. Soc. Lond.*, xxxiii. 34, 1892. (27) C. D. B. Hale and J. F. Goodhart, *Trans. Clin. Soc. Lond.*, xxvi. 105, 1892–93. (28) A. E. Giles, *Trans. Obst. Soc. Lond.*, xxxiv. 132, 1893. (29) P. Guttmann, *Berl. klin. Wchnschr.*, xxx. 33, 1893. (30) J. Ikeda, *Centrlbl. f. Gynäk.*, xvii. 1089, 1893. (31) B. Thompson Lowne, *Descriptive Catalogue of the Teratological Series in the Museum of the R. C. of Surgeons of England*, p. 123, 1893, Six cases. (37) R. J. Marshall, *Glasgow Med. Journ.*, xl. 34, 1893. (38) K. Abel, *Berl. klin. Wchnschr.*, xxxi. 84, 114, 1894. (39) Clozier, *Bull. de l'Acad. de méd.*, 3 s., xxxii. 646, 1894. (40) C. Debierre and O. Lambert, *Journ. de l'anat. et physiol.*, xxx. 609, 1894. (41) L. v. Dittel, *Centrlbl. f. Gynäk.*, xviii. 488, 1894. (42) Gessner, *Centrlbl. f. Gynäk.*, xviii. 824, 1894. (43) Hochstetter, *Bericht Charité-Annalen*, xix. 536, 1894. (44) C. S. Jaffe, *Trans. Path. Soc. Lond.*, xlv. 224, 1894. (45) L. Joly, *Bull. de la Soc. anat. de Par.*, 5 s., viii. 14, 1894. (46) H. T. Machell, *Med. News*, lxv. 389, 1894, Two cases. (48) A. Neumann, *Deutsche med. Wchnschr.*, xx. 661, 1894. (49) F. Meola and S. Bakunin, *Arch. di ostet. e ginec.*, i. 506, 1894, and ii. 27, 119, 1895. (50) F. A. Fry, *Montreal Med. Journ.*, xxiv. 101, 1895. (51) B. Lewy, *Deutsche med. Wchnschr.*, *Vereins-Beilage*, p. 11, Jan. 7, 1895. (52) A. J. M'Closky, *Lancet*, i. for 1895, p. 1116. (53) A. M. Paterson, *Proc. Anat. Soc. Gr. Brit. and Ireland*, p. 21, 1895, Two cases. (55) Schauta, *Centrlbl. f. Gynäk.*, xix. 348, 1895. (56) G. G. Sears, *Boston Med. and Surg. Journ.*, cxxxii. 107, 1895. (57) E. Mary P. Stone, *Austral. Med. Journ.*, n.s., xvii. 554, 1895. (58) Verdelet, *Journ. de méd. de Bordeaux*, xxv. 128, 1895. (59) A. Arnheim, *Diss. inaug.*, Giessen, 1896, Six cases. (65) Bonnet, *Dauphiné méd.*, xx. 278, 1896. (66) Chambrelent, *Journ. de méd. de Bordeaux*, xxvi. 483, 501, 1896. (67) A. Cocchi, *Ann. di ostet. e ginec.*, xviii. 497, 1896, Two cases. (69) G. Corrado, *Gior. di med. leg.*, iii. 9, 1896. (70) H. C. Fraker, *Columbus Med. Journ.*, xvi. 400, 1896. (71) A. E.

Maylard, *Glasgow Med. Journ.*, xlvi. 143, 1896. (72) E. Terrile, *Gazz. d. osp.*, xvii. 591, 1896. (73) C. Ogle, *Trans. Path. Soc. Lond.*, xlviii. 114, 1896–97. (74) W. D. Booker, *Arch. Pediat.*, xiv. 649, 1897. (75) H. Botesco, *Arch. d. sc. méd. . . . de Bucharest*, ii. 77, 1897. (76) Chambrelent and Princeteau, *Journ. de méd. de Bordeaux*, xxvii. 99, 1897. (77) A. H. Cordier, *Am. Journ. Surg. and Gynec.*, x. 114, 1897–98; and *Ann. Surg.*, xxvi. 353, 1897. (78) T. E. H. Fisher, *Lancet*, ii. for 1897, p. 1584. (79) P. I. Gautier, Paris, 1897, Five cases. (84) L. E. Holt, *Med. News*, lxxi. 769, 1897. (85) H. Hübl, *Centrlbl. f. Gynäk.*, xxi. 1353, 1897. (86) E. Barclay-Smith, *Journ. Anat. and Physiol.*, xxxii. 341, 1897–98. (87) G. Keim, G. Rosenthal, and Huguier, *Bull. Soc. d'obst.*, Par., p. 147, 1898. (88) A. J. Wood, *Intercolon. Med. Journ. Australas.*, iii. 96, 114, 1898. (89) O. Grosser, *Wien. klin. Wchnschr.*, xii. 655, 1899. (90) S. W. Kelley, *Arch. Pediat.*, xvi. 602, 1899. (91) E. Schwalbe, *München. med. Wchnschr.*, xlvi. 12, 1899, Four new cases, and one previously reported in *Morpholog. Arbeiten*, Bd. viii. 1898. (96) I. A. Abt, *Arch. Pediat.*, xvii. 261, 1900. (97) J. W. Ballantyne, *Physician and Surgeon*, i. 891, 1900; *vide* Plate XXIII. and Fig. 74. (99) L. Funck-Brentano, *Bull. et mém. Soc. anat. de Paris*, 6 s., ii. 537, 1900. (100) J. W. Ballantyne, Case of Iniencephaly with congenital diaphragmatic hernia, 1900, *vide* Plate XVI.

Malformations of the Sternum.

Both *cyphosis* and *lordosis* of the sternum occur as congenital anomalies; but considerable confusion has arisen as to which is lordosis and which cyphosis. Taruffi (*Storia*, vii. 175, 1894), for instance, defines lordosis as anterior convexity of the sternum, while cyphosis is anterior concavity; he thus regards the sternum as similar in this respect to the vertebral column. G. D'Ajutolo (*Memoria*, Bologna, 1898), however, looking to the etymology of the words, terms an anterior sternal convexity cyphosis and an anterior sternal concavity lordosis; but although this nomenclature is more correct in an etymological sense, I prefer to retain Taruffi's. Lordosis (anterior convexity of the sternum) is comparatively rare; but D'Ajutolo (*op. cit.*) has described four cases. These were all partial, and in three of them the lordosis was *superior* and one *inferior*; two of the three superior cases were in sisters; they were all present at birth. Sternal cyphosis (anterior concavity of the sternum) is far more common. In Germany this deformity has, since W. Ebstein's time (*Deutsches Arch. f. klin. Med.*, xxx. 411, 1881–82; xxxiii. 100, 1883), been termed *Trichterbrust*; and it is sometimes known in English as the funnel-shaped thorax. Cases had, however, been observed before Ebstein described it; thus Eggel (*Arch. f. path. Anat.*, xlix. 230, 1870), Flesch (*ibid.*, lvii. 289, 1873), and N. Hagmann (*Jahrb. f. Kinderh.*, n. F., xv. 455, 1880) had all reported instances; within the past twenty years many new observations have been added, so that the bibliography is now a large one (A. Grünenthal, *Diss. inaug.*, Berlin, 1888; W. Graeffner, *Deutsches Arch. f. klin. Med.*, xxxiii. 95, 1883; E. Coen, *Bull. d. sc. med. di Bologna*, 6 s., xiv. 7, 1884; F. Percival, *Riv. clin. di Bologna*, 3 s., iv. 401, 1884; G. Klemperer, *Deutsche med. Wchnschr.*, xiv. 732, 1888; J. Kundmüller, *Deutsche Arch. f. klin. Med.*, xxxvi. 543, 1884–85; H. Ribbert, *Deutsche med. Wchnschr.*, x. 533, 1884; H. R. Smith, *Norsk Mag. f. Lægevidensk.*, 4 R., i. 236, 1886; H. J. Vetlesen, *ibid.*, 4 R., i. 31, 1886, *Centralbl. f. klin. Med.*, vii. 745, 1886; E. Herbst, *Deutsches Arch. f. klin. Med.*, xli. 308, 1887; A. Frey, *Deutsche med. Wchnschr.*, xiii. 645, 1887; etc.). The concavity is generally in the middle line, and corresponds to the lower part of the sternum; in many respects it resembles the acquired form of the malformation seen in cobblers. Cyphosis and lordosis may be met with in the same case (*sternal cypho-lordosis* of D'Ajutolo). Heredity and family prevalence were not uncommonly noted (Smith, Vetlesen, Klemperer, Grünenthal, Herbst). Various causes have been alleged for sternal cyphosis, such as pressure of the fœtal heel (Hagmann), or chin (Ribbert), or fracture of the sternum from maternal traumatism in pregnancy (Graeffner), or shortness of the sternum (Ebstein), or rickets (Grünenthal). It is difficult to decide upon the most likely theory, but it is evidently a malformation which, from its nature, may arise in the fœtal period of antenatal life, although it may, as its hereditary character shows, be predisposed to earlier.

Sometimes *suprasternal ossicles* are detected along the upper margin of the sternum near the clavicular facets; these may be sesamoid in nature, or, more probably, they represent the epicoracoids of some animals. At the other extremity of the bone the *ensiform cartilage* may show such anomalies as *bifidity, absence*, and outward or inward *displacement*. Various anomalies in the construction and ossification of the sternum may be met with; one or two of the segments of the bone may remain separate and have fibro-cartilaginous tissue lying between them; there may be *supernumerary* ossific *nuclei*; or there may be one or (rarely) two *foramina* in the bone (Bogusat, *Diss. inaug.*, Königsberg, 1902). More important, however, than these malformations is congenital *fissure of the sternum*; this demands a paragraph to itself.

Fissure of the Sternum (Sternoschisis).

It is difficult to separate partial or complete absence of the sternum from fissure properly so called; thus, absence of the bone and a wide fissure of it (E. H. Martin, *Med. Rec.*, New York, xxxii. 425, 1887) may be practically indistinguishable; the two anomalies may, therefore, be considered together. On the other hand, cases in which there is ectopia of the heart (made possible by the divided state of the sternum) are best described by themselves.

No case of sternal fissure was ever so widely known as that of the man E. A. Groux, who travelled about from one European capital to another exhibiting himself. I have a pamphlet (*Abhandlungen und Notizen über E. A. Groux's Fissura sterni congenita*), published by the man himself at Hamburg in 1857, which contains the description of his malformation, with remarks thereupon by Hamernik, Baumgartner, Wagner, Beclard, Saint-Hilaire, Owen, Williams, Ernst, Sundewall, and many other medical men of the time. The great interest which Groux excited was not, however, due so much to the malformation as a malformation, but rather to the observations upon the action of the heart which it rendered possible. With these, although of great importance, we have not here to do. The fissure is generally V-shaped, wide above and narrow below, and is bridged across by fibrous tissue and the integuments. It may divide the whole bone from the manubrium to the ensiform; but occasionally it is restricted to one part, the manubrium being intact in some instances (W. Vrolik, *Tabulæ ad illustrandam Embryogenesin*, Pl. xxiv., Fig. 1, 1849), and the ensiform cartilage in others (O. Obermeier, *Arch. f. path. Anat.*, xlvi. 209, 1869), while in one curious case (that reported by L. Ramirez, *Gac. méd. de Mexico*, i. 217, 1867–68; *Gaz. méd. de Paris*, 3 s., xxiii. 66, 1868) there was a wide defect above and below, and a narrow fissure in the middle part of the bone. In the young man seen by G. A. Gibson and H. Malet (*Journ. Anat. and Physiol.*, xiv. 1, 1879–80) the fissure affected the manubrium sterni, and extended downwards to the level of the fourth costal cartilages; it measured about 1½ inch transversely in its upper part; and a strip of skin stretched upwards towards the sternum from the umbilicus for a distance of 3 inches. This second malformation (in the epigastric region) has been noted in other cases (Wittstock, *Monatschr. f. Med., Augenh. u. Chir.*, ii. 79, 1839; O. Obermeier, *loc. cit.*); and sometimes a cicatricial condition of the skin or an actual defect of the integument has been observed in the same region (Sebastiani, cited by Taruffi, *op. cit.*, vii. 187, 1894). Possibly both the sternal fissure and the deformity of the abdominal wall above the umbilicus originate in amniotic pressure, which arrests the development of the two lateral folds which grow together to close in the body cavity anteriorly. Ahlfeld (*op. cit.*, p. 177, 1882) suggests that the vitelline or umbilical duct may acquire adhesions with the pericardium, and so keep the original opening open or at least prevent its complete closure; he bases his theory on a case observed by him (*Arch. f. Gynæk.*, xii. 154, 1877), in which a filament resembling the vitelline duct was found attached to the thorax between the two mammary glands. It does not appear, however, that it is necessary to invoke such a mechanism, as simple pressure (amniotic or other) would appear to be sufficient to prevent the union of the two halves of the sternum.

Sternal Fissure with Ectopia Cordis.

In the previous chapter a brief reference was made to displacement upwards of the heart into the cervical region where there was a median fissure; as I shall have to point out later, a downward displacement of the heart occurs sometimes in connection with defect in the diaphragm and exomphalos (Fig. 28, p. 173); but the heart may also be dislocated forwards and come to lie outside of the chest through a defect in the sternum and anterior thoracic wall, and it is with this teratological state that I am here concerned.

In November 1896 I received a letter from Dr. G. F. Barnardo of Stepney, containing a description of a seven months' fœtus which lived six hours in an incubator. During that period it showed every sign of life, although the heart was lying outside the thoracic cavity, being suspended by a pedicle, springing from its base and running to the thoracic wall. The sternum was divided into halves, each bar being in relation to the sternal ends of the costal cartilages and consisting of a thin strip of cartilage, which was prolonged upward into the neck to articulate with the clavicle of the same side. The upper ends of the sternal bars were 2 inches apart and the lower ends 4 inches; through the opening thus produced the heart protruded. The pedicle contained the aorta, the pulmonary artery and veins, and the venæ cavæ. There was no pericardial sac, the visceral pericardium simply leaving the wall of the heart and being continued outwards for some distance, to blend finally with the skin of the body generally in a raised margin. The upper ends of the recti abdominis muscles were widely separated, but there were no other deformities. The ectopic heart had the structure which is normal at the seventh month of antenatal life; the lungs were normal, and each lay in its own pleural sac. It was noted that during life the apex of the heart at each systole was tilted right upwards so as to touch the infant's chin. This interesting case of ectopia cordis (extra-thoracic type) was afterwards figured and described both in the *British Medical Journal* (ii. for 1896, p. 1639) and in the *Journal of Anatomy and Physiology* (xxxii. 325, 1897–98).

Cases resembling Barnardo's are rare. According to the system of classification of C. Weese (*Diss. inaug.*, Berolini, 1818) they belong to the variety *ectopia cordis cum sterni fissura*; the other types are *ectopia supra-thoracica* (displacement of the heart upwards into the neck) and *ectopia sub-thoracica* (displacement downwards, by defect of the diaphragm, into the abdominal cavity or into the sac of an exomphalos). There has been a further subdivision of the variety with sternal fissure (also known simply as *exocardia*) into a superior, median, inferior, and lateral type, according as the displacement takes place in the upper, middle, or lower part of the bone, or at the side of the sternum altogether; but the number of observations is hardly large enough to justify such detail. Instances in which the sternal defect was superior, affecting the manubrium, were reported by E. Sandifort (*Acta Helvet.*, vii. 56, 1772), by S. Jones (*Trans. Path. Soc. Lond.*, vi. 98, 1855), and by H. Schlesinger (*Berlin. klin. Wchnschr.*, vii. 376, 1870). The heart was destitute of a pericardial sac, and in one instance (Schlesinger's) had a filamentous band attached to its apex (amniotic in origin?). Cases in which the heart protruded through a space formed by separation of the two halves of the sternum in their whole extent have been reported by Pecchioli (*Gaz. med. de Paris*, vii. 12, 1839), E. Daniell (*Brit. Med. Journ.*, ii. for 1860, p. 776), by H. J. Haan (*Diss. inaug.*, Bonnæ, 1825), and others. In these instances, and in others like them, the pericardial sac is generally absent or rudimentary; the heart itself may show no anomalies, but on the other hand it may have a bifid apex, incomplete interventricular and interauricular septa, two chambers instead of four, and no ductus arteriosus (Ranvier, *Compt. rend. Soc. de biol.*, 3 s., v. 93, 1864). Cases in which the heart protruded through an opening in the lower part of the sternum and of the epigastric region were seen by Ramel (*Journ. de méd., chir., pharm.*, xlix. 423, 1778), Chaussier (*Bull. Fac. de méd de Paris*, iv. 93, 1814), J. O'Bryen (*Trans. Prov. Med. and Surg. Assoc.*, vi. 374, 1838), von Gross and Heim (*Med. Cor.-Bl. d. württemb. ärztl. Ver.*, xxix. 229, 1859), E. Rezek (*Wien. med. Presse*, ix. 673, 1868), A. François-Franck (*Compt. rend. Soc. de biol.*, 6 s., iv. 340, 1879), and L. Ranvier (*loc. cit.*). In these sub-thoracic cases the pericardium may be present and the child may survive its birth for some time and even reach adult life. Sometimes the heart was contained in a thin-walled sac (amniotic or peritoneal), in which lay also (in some instances) the liver, stomach, and intestinal coils. Again, there have been cases in which the whole sternum was divided as well as the epigastrium; in them the anterior thoracic wall is open, and so is the abdominal as low down as the umbilicus. Taruffi (*op. cit.*, viii. 410, 1894) has collected together nine records of this sterno-epigastric type of ectopia cordis, including those of Grandi, Hammer, Fracassini, Weese, Locatelli, and Ahlfeld. Just as fissure of the sternum in its upper part may be unaccompanied by extrusion of the heart, so even in cases of fissure extending as low as the umbilicus and sometimes including it, cardiac displacement is not a necessary concomitant (*vide* p. 520). When we are considering such specimens as those of Grandi, Hammer, and Ahlfeld, we are really dealing with the connecting links which join one teratological type (fissure of the thorax) to another (fissure of the anterior abdominal wall); we pass from one group of cases in which division of the sternum and protrusion of the heart are the leading features to another in which defect of the anterior abdominal wall and protrusion of the abdominal viscera are the leading features, and between the two groups are the intermediate types which show these features combined in various ways.

The *teratogenesis* of ectopia cordis presents several difficult problems. It is a rare monstrosity both in the human subject and in mammals. It is not indeed unknown to the lower animals, cases both of *schisto-cormus fissisternalis* and of *schisto-cormus schistepigastrico-sternalis* having been recorded by Gurlt (*op. cit.*, ii. 132, 133, 1832); but it is uncommon enough to suggest that there must be some special reason therefor. Considering that there is a stage in ontogenesis when the heart is outside the body, it is obvious that the idea of arrested development offers a tempting solution of the problem of the causation of ectopia cordis. It may further be added that there is some evidence that this arrest is due to amniotic influences, traces of filaments and bands having been found in certain cases. Can we reconcile this theory with the rarity of the monstrosity? At first sight it would appear as if it ought to be a common instead of a rare type; but a little reflection and some investigation of early stages in the formation of the thorax show to us that there is only a brief period in ontogenesis during which the anterior aspect of the thorax is subject to amniotic influences; the natural flexed attitude of the embryo saves its anterior aspect from pressure, and possibly the presence of the developing upper limb-buds increases the protection. But, it may be urged, defective closure of the adjacent abdominal walls is common. This is admitted, but there is in that region a natural opening, the umbilicus, which does not permanently and entirely close till after birth, and there is no such complete protection by flexion of the trunk and the presence of limb-buds as there is higher up. It is, therefore, quite permissible to accept the theory of arrested development in ectopia cordis. There may be a complex action of the amnion to account for the arrest: amniotic pressure from non-separation of the amniotic membrane may prevent the fusion of the body walls in the middle line, and amniotic adhesions may hold the heart forwards. The fact that sometimes, as in François-Franck's patient (*loc. cit.*), there is no break in the continuity of the skin covering the displaced heart, introduces a difficulty; but it is possible that in such instances the amniotic pressure and adhesions may have been temporary and ceased soon enough to allow the thoraco-abdominal walls to close, albeit imperfectly.

Pleurosomus.

Just as fissure of the sternum may be either accompanied or unaccompanied by protrusion of the heart, so a lateral fissure of the chest-wall may or may not be associated with prolapse of the lungs (and heart) through it. I have already considered defects in the thoracic lateral wall unaccompanied by protrusion of the exposed viscera (p. 470); now the more grave type of defect with visceral displacement calls for description. Isidore Geoffroy Saint-Hilaire (*Histoire*, ii. 267, 1836) placed cases of lateral fissure of the chest among the celosomic monstrosities, and made a special genus for them under the name of pleurosomus; and he *defined* them as instances of lateral eventration affecting chiefly the upper part of the abdomen and extending to the thorax, and being accompanied by absence or incomplete development of the arm of the same side. Saint-Hilaire had an opportunity of examining two cases of pleurosomus, one in a calf, the other in a human fœtus; in both the left side was affected and in both the corresponding limb was practically absent; in the case of the human fœtus the umbilical cord, which was short, was adherent to the head, which was deformed (hyperencephaly). The left side is not invariably the affected one, as was demonstrated by the specimen which I showed to the Edinburgh Obstetrical Society in 1902 (*Trans. Edinb. Obst. Soc.*, xxvii. 112, 1901–02); the right arm was in this instance adherent to the margin of the thoraco-abdominal opening in the right side of the body (Fig. 34).

Sometimes the sheath of the umbilical cord can be recognised as continuous with the skin margins of the thoraco-abdominal opening; but there may be no true cord, or the sac walls may have been torn in labour. The sac may in some instances be covered with skin, or may be formed by the peritoneal membrane. There does not appear to be any known case in which the defect was limited absolutely to the thoracic wall; in all of the recorded instances the abdominal cavity was opened into; and in some (*e.g.* Campana's case, cited by Taruffi, *op. cit.*, vii. 210, 1894) the whole of the left side of the body from the crest of the ilium to the second rib, and from the margin of the sternum to the vertebral column, was wanting. We shall see, however, that a lateral opening in the abdominal wall may occur independently of any thoracic defect.

The arm of the affected side was generally deformed: it was a shapeless rudiment in Hertwig's case (*Diss. inaug.*, Landshuti, 1821) and a stump ending in one digit in Elsholt's specimen (*Miscel. Acad. nat. curios*, iv.–v., App. p. 80, 1676). In Campana's observation (*loc. cit.*) it was not only deformed (stump-like), but was abnormally placed, being curiously inserted upon the clavicle; in Reil's case (*Illust. med. Ztg.*, iii. 83, 1853) it was fixed to the cartilage of the sixth rib; and in Förster's specimen (*Die Missbildungen des Menschen*, Pl. xi. Fig. 16) it was situated near the sternum. It was absent altogether in the case reported by E. Martin and Letulle (*Journ. de l'anat. et physiol.*, xii. 561, 1876). The heart was nearly always extruded and lay on the top of the abdominal viscera (*e.g.* in Klein's case, *Deutsches Arch. f. d. Physiol.*, iii. 391, 1817), and in Campana's specimen (*loc. cit.*) the lungs, also, were among the displaced organs. The heart would appear to have been generally enveloped in the pericardium.

Various *associated malformations* have been recorded, such as hare-lip and facial fissures (Campana, *loc. cit.*), a tail-like projection (Elsholt, *loc. cit.*), encephalocele (C. Weese, *Diss. inaug.*, Berolini, 1818), and spina bifida, atresia ani, and absence of genitals (F. W. Voigtel, *Fragmenta semeiologiæ obstetriciæ*, Pl. v., p. 77, Halæ, 1790). The associated deformities do not throw much light upon the *teratogenesis* of pleurosomus of the thoracic region, which remains very obscure. It is indeed most difficult to account for lateral openings in the thoraco-abdominal parietes; for arrested development fails in such instances to be an easy method of explanation, there being no embryonic aperture which by its permanence can become the teratological defect. Any theory to be worthy of credence must take into account the associated anomalies of the arm of the affected side and the almost constant left-sided nature of the malformation. Possibly the primitive left-sided spirality of the embryo may be exaggerated and made permanent by amniotic adhesion and pressure, and an actual want of formation of the chest-wall take place in consequence of the pressure thus brought to bear upon it; but the causation is surrounded by great obscurity.

Thoracic Patagium.

Reference has already been made to the occurrence of a web of skin (patagium) in the cervical region (p. 460); and I note here that the same anomaly may occur in relation to the thorax. It consists of a fibrous band or fold of skin passing from the ribs to the humerus, and it is apt to be associated with defect of the pectoral muscles

(J. Thomson, *Teratologia,* ii. 8, 1895; Bruns and Kredel, *Fortschr. d. Med.,* viii. 1, 1890; R. Johnson, *Trans. Clin. Soc. Lond.,* xxxvi. 259, 1902–03). It is possible that the case reported by Hippocrates (Littre's *Œuvres complètes d'Hippocrate,* v. 213, 1846) of a dead-born infant having the right arm adherent to the thorax was an instance of thoracic patagium; if so, it is the earliest of which we have any account (*vide* my article in *Teratologia,* ii. 276, 1895).

CHAPTER XXVI

Merosomatous Terata (*cont.*): Malformations of the Thoracic Organs: Malformations of the Heart: Individual Anomalies of Interauricular and Interventricular Septa, Pulmonary Artery, Aorta, and Valves; Associations of Cardiac Anomalies; Associated Malformations; Teratogenesis; Symptomatology; Malformations of the Lungs, Trachea, Bronchi, and Thymus Gland.

Malformations of the Heart.

In the first volume of this work (p. 369) I discussed the relation of fœtal diseases, and more especially of fœtal endocarditis, to congenital malformations of the heart. I there endeavoured to disentangle the cardiac diseases arising in fœtal life from the cardiac malformations arising in embryonic life. For various reasons I was not completely successful, as the reader will realise if he will glance over the passage referred to. The chief difficulty arose on account of the peculiar mode of development of the heart. This organ passes through the phases of its ontogenesis early and quickly; at the end of the second month of antenatal life it is structurally as complete as when the infant is born; its malformations, therefore, must also arise early. But there is a portion of its ontogenesis which is postponed until birth; I refer to the closure of the foramen ovale and the ductus arteriosus. There is thus produced the unusual phenomenon of development divided into two phases, an early and a late, by an intermediate resting period of seven months; the construction of the heart reaches the stage necessary for the maintenance of healthy antenatal life at the second month, and it is not till the ninth that further structural alterations occur to fit it for the requirements of the postnatal circulation. The malformations of the heart, therefore, are divisible into two groups: there are those which arise early, such as absence of the interventricular septum, and are truly embryonic in time, and those which arise later, such as a perforate state of the foramen ovale, and are sometimes postnatal in character. Between these two periods it is necessary to think of the heart as subject to diseases, such as endocarditis, but as not in a state to develop malformations. It is easy, therefore, to see how complicated the question of the antenatal pathology of this organ becomes, and how fœtal diseases, embryonic malformations, and postnatal anomalies have come to be combined, not only in the minds of investigators, but in actual occurrence. Thus it happens that in Volume I. I discussed fœtal endocarditis and the malformations (unclosed foramen and perforate ductus arteriosus) which follow it in point of time, while in this volume (which deals with the embryo) I have to consider the earlier and more fundamental malformations of embryonic life; at the same time, since this mode of subdivision of the subject is somewhat unusual, I do not absolutely adhere to it, but permit myself to refer to postnatal as well as embryonic malformations. Fœtal endocarditis, as I have already explained in Volume I., is related both to the early and the late malformations: it may possibly occur more readily in a heart which is malformed in the embryonic phase of antenatal life; it probably is to some extent the cause of the malformations which arise at and immediately after birth.

From the theoretical standpoint it ought to be possible to arrange all the malformations of the heart in a chronological series according to the time when they develop. We have some knowledge of the state of development of the heart at the second, third, fourth, fifth, and sixth weeks of antenatal life (*vide* pp. 26, 31, 35, 48, 58, 67), and we ought, therefore, to be able to arrange the cardiac malformations in a series according to the week during which they were produced, for we should be able to recognise the stage of ontogenesis at which the arrest of development and the resulting structural anomaly occurred. As a matter of fact this is to some extent practicable: we know, for instance, that the separation of the ventricles is completed during the sixth week by the formation of the pars membranacea septi, and we are at liberty to conclude that perforations affecting the pars membranacea of the septum arise during this week of antenatal life. We are, however, prevented from forming a complete chronological arrangement of the cardiac malformations, partly by a want of exact knowledge regarding many of the earlier organogenetic phenomena, and partly by the overlapping of malformations, by the occurrence, for instance, of anomalies of different ages in the same heart. I shall, therefore, follow the usual plans of arrangement, and describe first the individual anomalies according to the parts affected, and second the most usual associations of these malformations.

Cardiac malformations have been ably discussed by various authors, among whom I may mention J. R. Farre (1814), J. Paget (1831), H. Friedberg (1844), T. B. Peacock (1864, 1866), C. F. von Rokitansky (1875), C. Taruffi (1875), C. Rauchfuss (in Gerhardt's *Handbuch der Kinderkrankheiten*, iv. 1877–83), E. Théremin (1895), H. Vierordt (1898), G. A. Gibson (1898), and A. Moussous (in Grancher's *Traité des maladies de l'enfance*, 2nd edit., iii. 708, 1904), leaving many others unnamed. In this chapter I have not to deal with all the teratological conditions which may affect the heart; for some of them, such as ectopia, have been described already, and others, such as absence (in acardiac fœtuses) and transposition, fall to be referred to later.

Anomalies of the Interauricular Septum.

The commonest congenital anomaly of this septum undoubtedly is incomplete closure of the foramen ovale, due to want of union of the membrane with the margin of the fossa. This, however, is not an embryonic but a postnatal malformation; it represents a state which is normal during the whole of antenatal life, but which is anatomically abnormal as soon as postnatal life begins. Even then it may not interfere with the physiological action of the heart so long as the membrane occupies the foramen (although unattached), for the pressure on one side of it is balanced by that on the other side; but in diseased states of the circulation, when the pressure in the right auricle exceeds that in the left auricle, the interauricular curtain may swing aside and allow mixing of the venous and arterial blood.

Other anomalies of the interauricular septum, however, arise at an early period in antenatal life, and give rise to morbid states which are truly embryonic and teratological. There is, for instance, complete absence of the whole septum, a rare anomaly; an example of it is said to have been reported by Méry in 1700. More common are the less or more extensive defects in the interauricular septum which have been described by many writers. In order to understand their nature and mode of origin it is necessary to remember that the formation of the septum between the auricles is somewhat complex: there is first a falciform ridge which runs dorso-ventrally across the roof of the originally single auricular cavity, and is known as the septum primum; it would soon, by its growth, separate the right and left auricles completely if a foramen (foramen ovale) did not appear in its dorsal portion; a second ridge (septum secundum) next develops in the roof and ventral wall of the right auricle, and becomes continuous with the fold guarding the opening of the sinus venosus; endocardial cushions then grow from the dorsal and ventral walls of the auricular canal, and uniting together divide this canal into a right and left half, and also join with the septum primum to complete the interauricular septum. Arrested development of either the primary or secondary septum may occur, and will result in the presence of an opening between the auricles. Thus, the septum primum may be little more than a ridge, when the opening between the auricles will be large; or there may be a less marked defect, the fossa ovalis may be open or shut, and a semilunar opening be found. Again, the secondary septum may be incomplete, when the opening is posterior in position and does not descend as low as the floor of the auricular cavity; there may be no traces of the primary septum, or it may be represented by a ridge, by a fenestrated membrane, by a band, or by a large open fossa ovalis. Many instances of these various conditions might be cited; but I shall refer here to only two or three. E. Théremin (*Études sur les affections congénitales du cœur*, p. 154, 1895) has described a case in which the interauricular septum was entirely absent; the two auricles formed a single cavity, into which the two venæ cavæ opened on the right side, and three pulmonary veins (of which one was double) on the left side; the common auricular cavity communicated with the two ventricles by a large opening divided into two by the interventricular septum. In another of Théremin's cases (*op. cit.*, p. 153), the foramen ovale was nearly closed by the membrane, and was separated from an opening in the interauricular septum by the Eustachian valve which formed a well-developed muscular band; the opening was triangular in shape and had the apex turned downwards, reaching the septum ventriculorum at the lower margin of the posterior wall of the conus arteriosus. In both these cases the muscular part of the septum was involved; but, of course, it is the membranous part in the foramen ovale that is most commonly defective; references to cases of the latter deformity might be multiplied almost indefinitely. A few references are appended, and the reader will find many more in the *Index Catalogue* of Washington (vol. v. p. 962, 1884; 2 s., vol. vi. p. 855, 1901): Anger, *Compt. rend. Soc. de biol.*, 4 s., i. 97, 1865; Blum, *Bull. Soc. anat. de Par.*, xliv. 246, 1869; Bucqoy, *Union méd.*, 3 s., xxx. 698, 1880; R. Caton, *Lancet*, ii. for 1878, 252; H. Chiari, *Jahrb. f. Kinderh.*, n. F., xv. 319, 1880; Ford, *N. York Med. Journ.*, xxv. 405, 1877; Geffrier, *France méd.*, xxviii. 254, 1881; C. Hüter, *Arch. f. path. Anat.*, xxx. 587, 1864; C. Lacroix, *Journ. Soc. de méd. prat. de Montpelier*, vii. 200, 1843; Landouzy, *Arch. gén. de méd.*, xlvii. 460, 1872; E. Malvoz, *Ann. Soc. méd.-chir. de Liége*, xxviii. 177, 1889; K. Rudolph, *Diss. inaug.*, Kiel, 1900; H. Ruge, *Diss. inaug.*, Berlin, 1891; L. Vincenzi, *Arch. per le sc. med.*, Torino, ix. 307, 1885–86; W. W. Wagstaffe, *Trans. Path. Soc. Lond.*, xix. 96, 1868.

Anomalies of the Interventricular Septum.

There is no normal aperture in the interventricular septum at the end of antenatal life, and all congenital openings here may, therefore, be regarded as embryonic malformations. The septum between the ventricles, like that between the auricles, is formed not of one but of several parts. It consists chiefly of a ridge (ventricular ridge) which arises from the floor of the single ventricular cavity; this grows more rapidly in its dorsal than in its ventral part, and so comes soon into contact and fuses with the dorsal part of the partition of the auricular canal, leaving an oval foramen in front just below the point where the aortic bulb arises. Another ridge, or rather two fused ridges, closes the above-mentioned opening and completes the septum ventriculorum; it is called the aortic septum, and serves also to divide the bulb into two vessels (aorta and pulmonary artery). A more detailed description of the interventricular septum recognises three parts, a posterior segment, an anterior segment (consisting in its turn of an anterior and a posterior part), and an intermediate membranous space ("undefended space"); all these parts can be seen along the upper part of the septum; the membranous space (pars membranacea septi) is derived from the aortic septum, and the other two (muscular portions) from the ventricular septum. Openings in the septum corresponding to all these various parts have been put on record, and A. Moussous (*Maladies congénitales du cœur*, p. 45, 1895) carefully distinguishes between them. There may, for instance, be an aperture at the centre or near the apex of the partition; such an aperture may be solitary, but more often there are several, and they are then mere pinholes in the wall; in these positions they are always rare. More common is it to find a notch at the base of the septum: it may affect the posterior segment and may include the membranous space and the posterior part of the anterior segment, producing a large opening; or the notch may affect the whole of the anterior segment (causing a wide aperture), or only its anterior part (causing a small round aperture), or, most commonly, its posterior part (producing a semilunar or triangular aperture large enough to admit the little finger, lying just below the aorta); or, finally, the perforation may lie in the membranous space. It was at one time thought that the membranous space was the commonest site for interventricular openings; but Rokitansky (*Die Defecte der Scheidewände des Herzens*, Wien, 1875) has shown that while this membrane is occasionally affected, either in its aortic or in its mitral part, or in both, it is more common to find the perforation in the posterior part of the anterior septum in the immediate vicinity of the membranous space. It may be noted, as a rare occurrence, that the whole interventricular septum or a very large part of it may be absent.

I may cite here some bibliographical references to cases of defect in the interventricular septum; the list is only representative: C. Assmus, *Diss. inaug.*, Leipzig, 1877; A. Béhier, *Bull. Soc. anat. de Paris*, xliv. 171, 1869; J. R. Bennett, *Trans. Path. Soc. Lond.*, i. 59, 1846–48; G. W. Callender, *ibid.*, ix. 91, 1857–58; Coale, *Boston Med. and Surg. Journ.*, liv. 18, 1856; S. Coupland, *Med. Times and Gaz.*, ii. for 1884, p. 501; G. Decaisne, *Bull. Soc. anat. de Paris*, lii. 445, 1877; D. Duckworth, *Journ. Anat. and Physiol.*, xi. 183, 1876; V. Eisenmenger, *Ztschr. f. klin. Med.*, xxxii. Supplhft., 1, 1897; R. Elliot, *Journ. Anat. and Physiol.*, xi. 302, 1877; J. P. C. Griffith, *Trans. Coll. Phys.*, Philadelphia, xviii. 152, 1896; S. O. Habershon, *Guy's Hosp. Rep.*, 3 s., xvii. 443, 1872; Herbst, *München. med. Wchnschr.*, xlviii. 368, 1901; L. E. Holt, *Arch. Pediat.*, vii. 81, 1890, xii. 839, 1895; C. Karsten, *Diss. inaug.*, Rostock, 1874; L. Lavergne, *Thèse*, Paris, 1886; A. Lombardini, *Gazz. d. osp.*, iv. 660, 1883; H. G. Mühsam, *Diss. inaug.*, Kiel, 1900; O. Müller, *Arch. f. path. Anat.*, lxv. 140, 1875; R. M. Olshausen, *Deutsche Klinik*, xxii. 7, 1870; Passow, *Charité-Ann.*, xix. 219, 1894; T. B. Peacock, *Trans. Path. Soc. Lond.*, v. 67, 1853–54; Polaillon, *Union méd.*, i. for 1876, p. 819; R. Quain, *Trans. Path. Soc. Lond.*, i. 60, 1846–48; H. D. Rolleston, *ibid.*, xlii. 65, 1890–91; W. H. Stone, *St. Thomas's Hosp. Rep.*, n.s., xi. 57, 1882; F. Taylor, *Guy's Hosp. Rep.*, 3 s., xx. 566, 1875; C. Vinay, *Lyon méd.*, xciv. 325, 1900; F. Willcocks, *Trans. Path. Soc. Lond.*, xxxviii. 96, 1886–87; Wittcke, *Journn. d. pract. Heilk.*, lxvi. 4 St., 38, 1828; R. Ziegenspeck, *Arch. f. Gynaek.*, xxxii. 111, 1888.

Anomalies of the Pulmonary Artery.

The commonest of all the congenital malformations of the heart is narrowing of the pulmonary artery. The *stenosis* may affect the valvular orifice itself, and then it is usually due to coalescence of the cusps; in this way a sort of diaphragm is produced, perforated at its centre; more rarely there is complete obliteration. It is also rare to find pulmonary incompetence; when it does occur it is usually due to rudimentary development or absence of the sigmoid valves. The stenosis, again, may affect the conus arteriosus or infundibulum; when this is the case and when the narrowing is low down, a sort of supplementary ventricular cavity is produced, and when it is in the middle part the infundibulum takes on an hour-glass shape; the defect may lead not only to narrowing but to shortening of the infundibulum, and there may even be complete absence of it. Finally, the stenosis may be above the level of the valvular orifice; there may be a uniform diminution in the calibre of the pulmonary artery up to the point of its bifurcation into its two branches, which may be normal in size or narrowed like the parent trunk. B. Zuber (*Jahrb. f. Kinderh.*, lix. 30, 1904) has reported a case of marked congenital *dilatation* of the whole pulmonary artery. These pulmonary defects rarely if ever exist alone; they are generally associated with septal defects, as will be shown immediately.

I append, as usual, a few out of the many bibliographical references which exist. O. H. Allis, *Phila. Med. Times*, ii. for 1872, p. 174; A. Bechtel, *Diss. inaug.*, Zurich, 1862; G. J. Bozanis, *Diss. inaug.*, Würzburg, 1876; Bohn, *Deutsch. Arch. f. klin. Med.*, v. 436, 1869; A. J. Burgess, *Med. News*, lxii. 437, 1893; F. Gatti, *Ann. univ. di med. e chir.*, ccxxxv. 305, 1876: A. P. Daniel, *Thèse*, Paris, 1874; A. Debely, *Thèse*, Montpellier, 1878; A. Hugues, *Thèse*, Paris, 1874; Kussmaul, *Ztschr. f. rat. Med.*, 3 R., xxvi. 99, 1866; H. Lebert, *Med. Times and Gaz.*, i. for 1870, p. 1; H. Meyer, *Arch. f. path. Anat.*, xii. 497, 1857; W. R. E. Smart, *Lancet*, ii. for 1871, p. 288; C. Taruffi, *Gior. d. r. Accad. di med. di Torino*, xxxviii. 257, 1875; S. Weiss, *Diss. inaug.*, Erlangen, 1874.

Anomalies of the Aorta.

Anomalies of the aorta are less common than those of the pulmonary artery, and when they do occur they are more often of the nature of dilatation than of stenosis. Congenital aortic dilatation is practically always associated with other malformations; and since, as Moussous (*op. cit.*) points out, there is generally an increase in the semilunar cusps as well as in the ring of the vessel, incompetence is uncommon. Aortic narrowing may exist as the sole malformation or in association with other defects. When it occurs alone (which is rare), it may affect the whole vessel and may possibly be an anomaly predisposing to chlorosis (Virchow); or it may be localised to the part of the vessel lying between the origin of the left subclavian artery and the insertion of the ductus arteriosus; or, again, it may be situated at the part where the ductus arteriosus enters the aorta, as is well shown by E. Wadstein in an inaugural dissertation of Lund (*Om stenos och obliteration af aorta vid eller i närheten af ductus Botalli*, 1897). Aortic stenosis may also exist along with other anomalies, and then it may be situated at the orifice (coalescence of the semilunar valves to form a diaphragm) or in front of it (conus or pre-orificial part), which is very rare. Complete obliteration of the aortic orifice has also been noted, but it, likewise, is rather rare; instances have been reported by Canton (*Trans. Path. Soc. Lond.*, ii. 38, 1848–49), C. Devilliers (*Union méd.*, 2 s., vii. 338, 1860), A. Meyer (*Med. Rec.*, New York, xxiii. 428, 1883), S. G. Shattock (*Trans. Path. Soc. Lond.*, xxxii. 38, 1881), and E. Apert (*Bull. Soc. anat. de Paris*, lxx. 683, 1895). Théremin (*op. cit.*, p. 125) has given details of seventeen cases of aortic stenosis; in all of them the infant was feeble and weakly at birth; in five of them there were signs of fœtal endocarditis in both ventricles. It is difficult to exclude fœtal disease as a factor in the causation of congenital aortic stenosis, and it must be admitted that some cases are not truly embryonic malformations but are the results of fœtal endocarditis. Théremin (*op. cit.*, p. 14) has also given notes of twenty-five cases in which the stenosis was limited to the isthmus of the aorta; in some of them there were likewise signs of fœtal endocarditis. A few further references to the literature of congenital aortic stenosis may be appended here. Moutard-Martin, *Bull. Soc. anat. de Paris*, xlix. 737, 1874; M. Stoll-Krotowski, *Diss. inaug.*, Berlin, 1873; Bülau, *Berlin. klin. Wchnschr.*, x. 217, 1873; H. Eppinger, *Vrtljschr. f. d. prakt. Heilk.*, cxii. 31, 1871; Knoevenagel, *Berlin. klin. Wchnschr.*, xv. 525, 1878; T. A. Wise, *Trans. Med. and Phys. Soc. Calcutta*, viii. pt. 2, 384, 1842; Potain, *Gaz. hebd. de méd.*, 2 s., xxix. 292, 1892; A. Laboulbène et P. Claisse, *Bull. et mém. Soc. méd. d. hôp. de Paris*, 3 s., vii. 945, 1890; C. B. Lockwood, *St. Barth. Hosp. Rep.*, xiv. 352, 1878; E. Leyden, *Charité-Ann.*, xiv. 151, 1889.

Transposition of Aorta and Pulmonary Artery.

Minor anomalies may occur in the relations of the aorta and pulmonary artery to each other—the two trunks may lie too exactly side by side, or one may be too much in front of or behind the other—but the most important malformation with which we meet is transposition, the aorta arising from the right ventricle and the pulmonary artery from the left. W. Osler (Keating's *Cyclopædia of the Diseases of Children*, ii. p. 760, 1889) describes a fairly typical instance of transposition of these vessels; it was an eighth-month fœtus, which had also hydrocephalus, umbilical hernia, spina bifida, and club-feet; from the right cardiac ventricle, which was larger than the left, a vessel was given off, which passed over a vessel emerging from the left ventricle, and, crossing the left bronchus, descended as the thoracic aorta; just above its origin it gave off a small pulmonary branch to the imperfectly developed lungs; the left ventricle was smaller than the right, and from it a vessel passed up on the trachea without communicating with the vessel from the right ventricle, and then divided into the innominate and left carotid arteries; there was a small orifice in the septum ventriculorum. In other cases the transposition is more complete than what is described above, for the artery for the lungs may come from the left ventricle instead of from a vessel which afterwards becomes the descending aorta. A few references are added. F. Ducrest, *Arch. gén. de méd.*, iii. 76, 1840; J. H.

Smith, *Journ. Anat. and Physiol.*, xvi. 302, 1881–82; I. Etlinger, *Med. otchet Imp. S.-Peterb. Vosp. Doma*, 147, 1881; E. Termen, *ibid.*, 218, 1872; H. Ashby, *Journ. Anat. and Physiol.*, xvi. 90, 1881–82; M. Holl, *Med. Jahrb.*, 503, 1882; T. W. King, *Month. Journ. Med. Sc.*, iv. 32, 1844; D. B. Lees, *Trans. Path. Soc. Lond.*, xxxi. 58, 1879–80; L. Mazzotti, *Riv. clin. di Bologna*, 2 s., ix. 257, 1879; T. B. Peacock, *Trans. Path. Soc. Lond.*, vi. 117, 1855; P. H. Pye-Smith, *ibid.*, xxiii. 80, 1872; O. Ward, *ibid.*, iii. 63, 1850–51; F. H. T. Ramm, *Diss. inaug.*, Kiel, 1899; A. Coyon, *Bull. Soc. anat. de Paris*, lxxii. 519, 1897; J. Dorning, *Arch. Pediat.*, vii. 741, 1890; G. Sanders, *Journ. Anat. and Physiol.*, xxvii. 464, 1892–93; H. D. Rolleston, *Pediatrics*, iv. 108, 1897; Simmonds, *Deutsche med. Wchnschr.*, xxvi., *Ver.-Beil.*, 81, 1900.

Other Anomalies of the Great Vessels.

Either the aorta or the pulmonary artery may be absent completely, or, more often, may be represented solely by a fibrous band or cord. In these cases a single large trunk arises from the base of the heart; it may contain three or four semilunar valves; and it may or may not be subdivided internally into two passages by a septum. There is here evidently a persistence of a stage, normally transitory (truncus arteriosus communis), in which the aortic bulb is single, or, at any rate, double only in its interior. As a rule, this aortico-pulmonary vessel, as it has been called, is single only for a short distance (during which it gives origin to the coronary arteries), and then divides into an aorta and a pulmonary artery; in other instances, two pulmonary arteries, right and left, arise directly from it; in yet other cases, the lungs receive their blood supply from the greatly enlarged bronchial arteries (*vide* L. Muhr's *dissertation* of Würzburg (1889) and W. Pitschel's *dissertation* of Königsberg (1897)).

Persistence of the ductus arteriosus as a channel of communication between the pulmonary artery and aorta is a common anomaly; it is to be grouped with patency of the foramen ovale as a postnatal malformation. In some very rare instances, however, there is no ductus arteriosus, and the aorta and pulmonary artery simply communicate directly (*vide* L. Cazin's *Thèse*, Paris, 1897).

Various anomalies affecting the great veins of the thorax may be met with. Thus, either the superior or the inferior vena cava may open into the left auricle, while the pulmonary veins open into the right; again, either of them may open into both auricles (Dubrueil, *Mémor. d. hôp. du midi*, ii. 224, 1830). A pulmonary vein may open into the superior vena cava (W. Gruber, *Arch. f. path. Anat.*, cii. 3, 1885). Either the vena cava inferior or the vena cava superior may be double; this anomaly has been reported with comparative frequency. Instances of duplicity of the superior vena cava have been reported by Chassaignac (*Bull. Soc. anat. de Paris*, xv. 106, 1840), by Eppinger (*Mitth. d. Ver. d. Aerzte in Steiermark*, xxvi. 144, 1890), by W. Gruber (*Oesterr. Ztschr. f. prakt. Heilk.*, xi. 1115, 1865, xii. 556, 1866; *Arch. f. path. Anat.*, lxxxi. 462, 1880, xcix. 492, 1885), by R. Howden (*Journ. Anat. and Physiol.*, xxi. 72, 1886–87), by

H. Rex (*Prag. med. Wchnschr.*, vii. 341, 1882), and by Shepherd (*Med. News*, xlii. 694, 1883). Duplicity of the inferior vena cava has been noted by Lagneau (*Bull. Soc. anat. de Paris*, xxviii. 344, 1853) and Broca (*ibid.*, xxvii. 474, 1852), and partial duplicity of it by N. Nicolai (*Diss. inaug.*, Kiel, 1886) and by J. Walter (*Diss. inaug.*, Erlangen, 1884). Again, there may be a persistent left superior vena cava, the corresponding vessel on the right side being represented by a fibrous cord (J. J. Charles, *Journ. Anat. and Physiol.*, xxiii. 649, 1888–89); or the right superior vena cava may be absent (W. S. Greenfield, *Trans. Path. Soc. Lond.*, xxvii. 120, 1875–76). The presence of a left inferior vena cava has been noted by H. J. Waring (*Journ. Anat. and Physiol.*, xxviii. 46, 1893–94), by W. H. White (*Trans. Path. Soc. Lond.*, xxxv. 131, 1883–84), and others. Most of these anomalies are easily accounted for by persistence of transitory states, *e.g.* the left duct of Cuvier. Sometimes the pulmonary veins are abnormal in number; three or five have been met with.

Transposition of the thoracic duct has been observed. W. J. Walsham found it ending on the right side in the confluence of the internal jugular and subclavian veins (*St. Barth. Hosp. Rep.*, xvi. 99, 1880); and Calori (*Mem. d. r. Accad. d. sc. d. Ist. di Bologna*, 5 s., i. 189, 1890) noted that it passed into the right subclavian vein by two tubes, of which the larger was external to the jugular vein and the smaller posterior to it. G. Cousin's series of cases of anomalous arrangement of the duct was published in *Marseille médicale* (p. 334) in 1898; I summarised his article in the *Archives of Pediatrics* (vol. xv. p. 685, 1898).

Valvular Anomalies of the Heart.

Some of the congenital anomalies of the valves of the heart are doubtless due to fœtal endocarditis, but others are apparently of embryonic origin and of the nature of malformations. To some of these, allusion has already been made in the description of aortic and pulmonary narrowness and dilatation. The semilunar valves of the *aorta* and *pulmonary artery* may be diminished in number: they may all be absent; there may be two instead of three, and then there is usually stenosis of the affected vessel, aorta or pulmonary artery. Sometimes, although rarely, the number of the cusps is increased; there may be four or five of them, and they are more often found in connection with the pulmonary artery than with the aorta; they may be all of the same size, or one or two may be small or rudimentary. Sometimes the cusps are fenestrated. Details of individual cases will be found in the following references:—R. Albrecht, *St. Petersb. med. Wchnschr.*, i. pt. 24, 1, 1876; Bernard, *Bull. Soc. anat. de Paris*, lv. 426, 1880; C. H. Carter, *Trans. Path. Soc. Lond.*, xxiv. 48, 1873; Duckworth, *ibid.*, xvii. 113, 1866; Fletcher, *Prov. Med. and Surg. Journ.*, p. 270, 1849; E. H. Greenhow, *Trans. Path. Soc. Lond.*, xx. 98, 1869; W. Jenner, *ibid.*, iv. 102, 1852–53; Guéneau de Mussy, *Bull. Soc. anat. de Paris*, xi. 74, 1836–37; W. Osler, *Montreal Gen. Hosp. Rep.*, i. 284, 1880; Paulicki, *Deutsche Klinik*. xxi. 363, 1869;

O. Lindenberg, *Diss. inaug.*, Würzburg, 1893; E. Zollikofer, *Diss. inaug.*, Zurich, 1899; H. W. Cattell, *Trans. Path. Soc. Phila.*, xv. 161, 1889–91; G. Martinotti, *Gazz. d. clin.*, Torino, xxiii. 273, 289, 305, 1886, xxiv. 161, 1886; F. A. Packard, *Trans. Path. Soc. Phila.*, xiii. 100, 1885–87, xviii. 215, 1898; H. K. Abbott, *Journ. Anat. and Physiol.*, xxxviii. 103, 1903–04.

Anomalies of the auriculo-ventricular valves (mitral and tricuspid) may also be met with; but they are rare and are generally associated with other malformations (*e.g.* defective septa). Thus the three cusps of the tricuspid may be fused together, producing narrowing or actual obliteration of the orifice (W. G. MacCallum, *Johns Hopkins Hosp. Bull.*, xi. 71, 1900); similar changes have been met with in the two cusps of the mitral. Many of the reported cases are doubtless fœtal in origin (fœtal endocarditis), but some may be truly embryonic. The following references may be consulted:—E. T. Bruen, *Trans. Path. Soc. Phila.*, xiv. 154, 1891; J. J. D. Burns, *Brit. Med. Journ.*, i. for 1860, p. 301; A. L. Carroll, *Med. Rec.*, xv. 57, 1879; W. Ebstein, *Arch. f. Anat. Physiol. u. wissensch. Med.*, 238, 1866; W. S. Greenfield, *Trans. Path. Soc. Lond.*, xxvii. 128, 1876; C. Kelly, *ibid.*, xxi. 91, 1870; T. Marxsen, *Diss. inaug.*, Kiel, 1886; H. Matthiessen, *Diss. inaug.*, Kiel, 1896; H. O. Sommer, *Phila. Med. Journ.*, i. 528, 1898.

Associations of Cardiac Anomalies.

I have enumerated the more important individual malformations of the heart which are produced in early antenatal life; but it has to be recognised that these rarely occur alone, being generally combined together in certain ways. It must not, at the same time, be thought that they only occur in combination, for perforations of the interauricular and interventricular septa, narrowing of the pulmonary artery and aorta, transposition of these great vessels, and numerical anomalies in the cusps of the cardiac orifices may all be met with as solitary malformations. So, also, may persistence of the foramen ovale or of the ductus arteriosus, a fact which is readily understood when it is borne in mind that these anomalies are developed late in antenatal or early in postnatal life, at quite a different time from the others. Nevertheless, the outstanding character of cardiac anomalies is their tendency to be combined together in different ways; it is exceptional for them to occur singly. In many cases the associated malformations make it possible for both antenatal and postnatal life to be continued, and may restore the physiological equilibrium of the heart's action. Thus in Coyon's case (*Bull. Soc. anat. de Paris*, lxxii. 717, 1897), a child of thirteen months, both the pulmonary artery and the aorta sprang from the right ventricle, but then there was very little interventricular septum. It is indeed often a cause of wonder to the pathologist how far the heart can adapt itself to circumstances; thus, in another patient of Coyon (*loc. cit.*, p. 519) there was complete transposition of the pulmonary artery and the aorta, so that the right heart supplied the greater and the left the lesser circulation, for there was no defect in the interventricular septum; yet the child lived to the age of fourteen months, although it was always more or less cyanosed; there was some mixture of blood, however, through the patency of the foramen ovale and ductus arteriosus.

Let us look, now, more particularly, at some of the combinations or associations of cardiac anomalies.

There may, for instance, be the two-chambered or bilocular heart, in which defect of the interauricular septum is accompanied by defect of the interventricular septum, and a single large arterial trunk arises from the organ. This grouping of grave defects may be met with in markedly malformed twin fœtuses (*e.g.* the fœtus paracephalus dipus cardiacus, *Trans. Edinb. Obst. Soc.*, xviii. 103, 1893), which do not survive birth. On the other hand, it may occasionally be compatible with a certain degree of postnatal life; thus, W. P. Northrup's patient (*Med. Rec.*, New York, xxxiii. 353, 1888) lived for one month in a state of marked cyanosis, although the heart consisted of no more than two chambers, and the pulmonary artery was represented by a fibrous string. This grave type of malformation has sometimes been termed the "reptilian" heart.

A more common variety of association is the complete absence of the interventricular septum along with incomplete absence of the interauricular one (or *vice versâ*), and it is not uncommon to find, in addition, such anomalies as absence or stenosis of one or other of the great arterial trunks, with, perhaps, transposition of the aorta and pulmonary artery. Such combinations of grave cardiac anomalies may be accompanied by malformations in other parts of the body (*e.g.* anencephaly, exomphalos, etc.). Numerous instances have been put on record, of which I may refer to Epstein's case (*Ztschr. f. Heilk.*, vii. 308, 1886), in which the interventricular septum was absent, the interauricular incomplete, the pulmonary veins opened into the superior vena cava and the right auricle, the aorta was on the right side, and the spleen and omentum were absent. Notwithstanding the grave nature of their malformations, individuals thus affected may survive their birth, dying ultimately from such maladies as tubercle and cancer.

Associations of defects in which the number of anomalies is more restricted are more common than any of the foregoing. Thus the posterior part of the interventricular septum may be absent, when it is commonly found that the interauricular septum is perforated inferiorly and that there is some deformity of the auriculo-ventricular valves, along with dilatation of the right side of the heart and of the pulmonary artery; the foramen ovale may be open or closed. Again, the whole of the anterior part of the interventricular septum may be wanting, when there may be transposition of the aorta and pulmonary artery or fusion of these two vessels into one trunk. Yet again, the defect in the interventricular septum may lie in the posterior part of the anterior segment (usually regarded as coinciding with the "undefended space"); then there may be various combinations of deformities. For instance, there may be narrowing of the orifice of the pulmonary artery or of the whole vessel with dilatation of the aorta; or the pulmonary artery may be obliterated, when there is either persistence of the ductus arteriosus or a special enlargement or increased number of the bronchial arteries; rarely the association is with aortic instead of pulmonary stenosis; in all these types the semilunar valves of the aorta or pulmonary artery may be diminished to two instead of three, and the mitral and tricuspid valves may be deformed.

Partial defects of the interauricular septum are, as have been already described, of various kinds, according as the part which is wanting belonged to the primary or to the secondary septum or to both; they may be associated with partial absence of the interventricular septum, with (very often) dilatation of the pulmonary artery, and (rarely) with premature closure of the foramen ovale. When a single arterial trunk arises from the heart, other anomalies are always present, but they vary so much that no association of them can be regarded as typical. On the other hand, transposition of the aorta and pulmonary artery may be found as the solitary cardiac anomaly.

The associations of the cardiac malformations which are developed later in antenatal life (namely, patency of the foramen ovale and of the ductus arteriosus) are fairly typical. The open ductus and foramen may, for instance, exist apart from other anomalies; but more frequently an open foramen implies pulmonary stenosis, with, as a rule, obliteration of the ductus arteriosus. Again, patency of the foramen ovale may coexist with obliteration of the pulmonary artery, when, of course, the ductus will remain pervious.

Associated Malformations.

Besides the association together of various kinds of cardiac defect it remains to be noted that such anomalies are often combined with malformations outside the heart. It would appear that there are few monstrosities and malformations which may not be met with in association with cardiac anomalies, although precise evidence is not always forthcoming on account of the neglect to examine the internal organs in all cases. O. Schäffer (in F. von Winckel's *Berichte und Studien*, p. 515, 1892), who made careful dissections of all his teratological specimens, found, in one case, absence of the interventricular septum and transposition of the great vessels combined with umbilical hernia, club-foot, and absence of the right kidney and suprarenal capsule; in another instance, there were various defects (caudal appendage, club-hand, absence of fibula, anal atresia, and absence of the urinary organs) as well as two openings in the interventricular septum, the upper of which established a communication between the right ventricle and the left auricle. While such associations are common in fœtuses so malformed as to be incapable of postnatal life, they are also frequent in children not so fatally defective, as is shown by the fact that three out of nine cases of congenital heart disease reported by J. Thomson and W. B. Drummond (*Edinb. Hosp. Rep.*, vi. 57, 1900) exhibited defects in other parts of the body (*e.g.* hare-lip, cleft palate, digital and aural anomalies, imperforate anus). F. Warner (*Med. Times and Gaz.*, i. for 1882, 61, 90, 144) gave many illustrative instances of the same association of anomalies in 1882. P. Hébert (*Rev. d'orthop.* 2 s., v. 57, 1904) has described an infant, one month old, in whom there was absence of the bile ducts, absence of the radius, club-hand, dislocation of the shoulder, and a congenital malformation of the heart (open foramen).

Teratogenesis.

The cardiac anomalies present many difficulties, not the least of which are concerned with their causation. I do not pretend to be able to solve these difficulties; I have already tried to throw some light upon some of them in the first volume of this Manual (pp. 369–373), although not, I fear, with shining success. All that I can do here is to throw out some suggestions which may possibly open up new lines of inquiry which other investigators may profitably follow.

It may be thought that since the malformations of the heart are internal, lying as they do within the thoracic cavity, they are not under the influence of and cannot be caused by external morbid agencies. The same supposition might be made regarding malformations of the brain and spinal cord. It would, in this latter instance, be met with the statement that there is a time in the development of the nervous system when it is external and not internal. Similarly there is a time when the heart is outside the body of the developing embryo and not inside it. If therefore such external anomalies as facial fissures, exomphalos, anencephaly, and hemimely are to be explained by a teratogenic cause external to the embryo (although probably internal to its annexa), then there is no sufficient reason against the possibility of the malformations of the heart being also produced in their first inception by an external cause. We are not compelled to look only for an internal causative agency, such as fœtal endocarditis, although we may still regard such an etiological factor as a possibility. It is, further, unnecessary for us to think it impossible that the same causes as are in action in producing external malformations may be also in action in the development of cardiac defects. There may be a unity in teratogenesis after all, although the heart lie deeply buried in the interior of the fully formed embryo. There is a side argument which may be used in support of this conclusion, although too much stress need not be laid upon it. I refer to the frequent association in the same subject of internal anomalies of the heart with external malformations of the body, head, and limbs.

When we come to study the actual mechanism by which cardiac anomalies are produced, we are again surrounded by difficulties. If we have recourse to the most acceptable teratogenic theory, that which regards malformations as arrested developments, we get an explanation, fairly intelligible and fairly satisfactory, for such anomalies as absence of the interventricular septum, the presence of a truncus arteriosus communis, and a rudimentary state of the cusps of the cardiac orifices. Further, if we examine very minutely into the details of the various stages of the ontogenesis of the heart, as Rokitansky did in so illuminating a fashion, it begins to be clear that even such apparently inexplicable teratological states as transposition of the great vessels and anomalies of the large veins may be explicable in a similar manner. But there are yet other anomalies, such as pulmonary stenosis, aortic dilatation, and the deformities of the auriculo-ventricular valves and of the foramen ovale which seem to offer themselves for explanation by means of the theory of fœtal endocarditis or some other disease of the unborn infant. I have elsewhere given reasons for doubting the correctness of the notion that malformations are due to fœtal diseases (pp. 164–197), chief among which is the belief that the malformations precede the diseases; but I do not feel that such influences as fœtal endocarditis have no bearing at all upon the malformations which are found in the heart. The disease may attack the deformed part; it may even do so more readily because it is deformed; it may exaggerate the effects of the deformity, may prolong its existence, or, possibly, interfere with its antenatal cure; and it is not impossible that both the disease and the deformity may be caused by the same morbid agency, and that the difference in result may be due to the time when that agency comes into action. I need not, however, re-argue to its conclusion this matter of the nosological *versus* the embryological theory of teratogenesis, for that has been done once and for all in Chapter XI. All that I need add is a belief in its applicability to internal malformations of the heart as well as to external malformations of the head and trunk.

The ultimate cause of the arrest of development which leads to a cardiac malformation is obscure. Syphilis, rheumatism, alcoholism, tuberculosis, and lead poisoning in the parents have all been suspected of being the ultimate teratogenic cause; and it is quite conceivable that such poisons by their presence in the tissues of the early embryo may so influence its organogenesis as to cause arrests and disorders which are translated into anomalies and malformations in later antenatal life. To some extent, clinical evidence supports this conclusion; family prevalence has been noted several times in connection with congenital anomalies of the heart (Eger, *Deutsche med. Wchnschr.*, xix. 81, 1893; T. S. Dabney, *Proc. Orleans Parish Med. Soc.* (1896), p. 124, 1898; L. Ferrannini, *Arch. ital. di med. int.*, iii. fasc. 3–6, p. 65, 1900; A. Borgherini, *Gazz. d. osp.* xxi. 1415, 1900); and in many cases the parents of infants with such malformations have suffered from syphilis, tuberculosis, and the like. The supposition is, I think, warranted, that a poison, such as that of syphilis or tuberculosis, may by its presence in the embryonic tissues first cause arrested development and consequent embryonic malformations (defect of interventricular septum, etc.), may then produce fœtal endocarditis in the fœtal period of antenatal life, and may finally interfere with the closure of the foramen ovale and ductus arteriosus in early postnatal existence.

Antenatal Symptomatology of Cardiac Anomalies.

I have already (in Vol. I. p. 372) dealt with the possibility of diagnosing antenatal cardiac anomalies before birth by the detection of murmurs; I need not touch upon that subject again, save to add two references, namely, those of H. Barth (*France méd.*, xxvii. 353, 1880) and of C. Audry and E. Lacroix (*Lyon méd.*, lxiii. 341, 1890). When we come to ask ourselves the question, What effects upon the fœtal circulation and economy does an antenatal cardiac malformation produce? we enter upon an inquiry which is full of difficulty. I shall venture no more than a few general statements, which are of the nature rather of interrogations than of affirmations. In the first place, it is extremely likely that many antenatal lesions of the heart interfere little or not at all with the life and growth of the fœtus. Many cases are on record in which, after birth, congenital heart anomalies have existed for years without being suspected, and it is, therefore, quite probable that the same thing may occur in utero. What makes this the more likely is the character of the fœtal circulation: even under normal circumstances there is such a mixture of pure arterial and impure venous blood that no part of the fœtus gets a much better supply than any other part, except, perhaps, in the case of the liver; the further mixing which may follow the presence of a defective interventricular septum is not, therefore, of high importance. In the second place, there seems to be no reason to doubt that the heart may attain to antenatal compensation. This may differ in detail from the compensation of postnatal life, but it cannot be more difficult of attainment, and may be very much easier if we consider the protective mechanisms of antenatal existence. Probably there is evidence of its occurrence in the fact that certain cardiac anomalies, such as narrowness of the pulmonary artery, are so often accompanied by associated malformations, such as defective interventricular and interauricular septa. In the third place, there is some evidence that cardiac anomalies occasionally have a grave effect upon antenatal life. Thus, it is no uncommon observation to note that infants thus affected are puny and delicate at birth. Further, fœtal ascites and general fœtal dropsy may sometimes be traced to such a cause. Hardouin and Moreau (*Rev. obstét. internat.*, suppl., p. 184, 1895), for instance, have recorded a case of ascites, hydrothorax, and general cyanosis in which there was no interauricular septum and only an imperfect interventricular one; and it has been maintained by some that premature closure of the foramen ovale may be the occasional cause of general fœtal dropsy (*vide* Vol. I. of this Manual, p. 295). It is quite likely that hydramnios may sometimes be due to circulatory disturbances in the fœtus. There are many other problems concerned with the effects produced upon fœtal life and health by a malformed heart—there is, for instance, the bearing of such a state upon the characters and number of the blood corpuscles, red and white—but I have already led the reader far enough into a region of surmises. With the much less shadowy subject of the postnatal symptoms, diagnosis, and treatment of congenital heart affections I have not, in this work, to do.

Malformations of the Lungs.

Malformations of the lungs are uncommon, and when they do occur are usually of the nature of accessory lobes (G. Humbert, *Rev. de méd.*, xxiv. 453, 1904). Normally the left lung consists of two and the right of three lobes; but the left may possess three lobes (*e.g.* in the cases of L. Humphry, *Journ. Anat. and Physiol.*, xix. 345, 1884–85, and of C. Giorgieri, *Gazz. d. osp.*, vii. 259, 1886), or the right may possess four (*e.g.* in the cases of J. Chiene, *Journ. Anat. and Physiol.*, iv. 89, 1870; of W. A. Edwards, *Amer. Journ. Med. Sc.*, n.s., xc. 182, 1885; of W. T. Eckley, *Chicago Med. Times*, xxvii. 201, 1895; and of Apert, *Bull. Soc. anat. de Paris*, p. 154, 1898) or even six lobes (Testut et J. Marcondès, *Gaz. hebd. d. sc. méd. de Bordeaux*, i. 1045, 1880). In Apert's specimen, which came from a man thirty-five years of age, the four lobes were produced by the presence of an X-shaped fissure instead of the normal Y-shaped one. Isolated accessory lobes may also be met with at the apex (E. W. Collins, *Dublin Journ. Med. Sc.*, lviii. 252, 1874) or at the base of the lung (E. Rektoržik, *Wchnbl. d. k. k. Gesellsch. de Aerzte in Wien*, xvii. 4, 1861). G. Schaffner (*Arch. f. path. Anat.*, clii. 1, 1898) believes that the lobus inferior accessorius is a fairly constant structure in both lungs, that on the right side it is constantly connected with the cardiac bronchus alone (being, therefore, homologous with the cardiac lobe of animals), while on the left side it is connected with the inner branch of the second ventral bronchus; the cardiac bronchus is an independent lateral bronchus, only occurring on the right side. The vena azygos major in a fold of the pleura may be found in the fissure which separates off a supernumerary lobule of the lung (W. Gruber, *Arch. f. path. Anat.*, lxxxi. 475, 1880; ciii. 484, 1886). An interesting article on this subject is that by R. de Josselin de Jong (*Nederl. Tijdschr. v. Geneesk.*, ii. for 1893, p. 669.

Incomplete development of one or both lungs is not very rare, and is chiefly associated with congenital diaphragmatic hernia (*q.v.*, p. 484). *Absence* of both lungs is sometimes met with, but only in grossly deformed twins (acardiac or acephalic); but absence of one lung may apparently occur and yet permit postnatal life. Maschka (*Allg. Wien. med. Ztg.*, vii. 78, 1862) recorded a case in which the right lung was absent, the whole of the right pleural cavity being filled by the heart; the right pulmonary vessels were absent, and the right bronchus was represented solely by a small cul-de-sac; the left lung consisted of only one lobe; the infant, a seven-months fœtus, lived for two hours. Hein (*Wchnschr. f. d. ges. Heilk.*, 536, 1837) also described a case of absence of the right lung; there was an opening in the interventricular septum of the heart. Absence of the left lung has been reported by Münchmeyer (*Deutsche med. Wchnschr.*, xi. 295, 1885), E. Théremin (*Rev. mens. d. mal. de l'enf.*, ii. for 1884, p. 554), and W. Gruber (*Arch. f. path. Anat.*, cii. 11, 1885). In the last-named case there were three supernumerary spleens and an accessory hepatic lobe. L. Fürst, in his valuable article on malformations of the lungs (in Gerhardt's *Handbuch der Kinderkrankheiten*, iii., 2 Hefte, 553, 1878), refers to a man seen by Haberlein who lived to the age of twenty years, although the left lung was absent. Another case of absence of the left lung in an adult was reported by M. Tichomiroff (*Month. Internat. Journ. Anat. and Physiol.*, xii. 24, 37, 1895); in this case there also was persistence of the left superior vena cava.

In connection with pulmonary malformations I may refer here very briefly to some *bronchial* and *tracheal anomalies.* The trachea may divide not into two but into three chief or stem bronchi. Cases have been reported by E. Leudet (*Compt. rend. Soc. de biol.*, 2 s., iii. 54, 1857), by D'Ajutolo (*Mem. r. Accad. d. sc. d. Ist. di Bologna*, 4 s., vi. 449, 1884–86), and by H. Chiari (*Ztschr. f. Heilk.*, x. 470, 1889; *Beitr. z. path. Anat. u. z. allg. Path.*, v. 329, 1889; *Prag. med. Wchnschr.*, xv. 567, 1890; xvi. 87, 1891). One of Chiari's cases was specially interesting. It was that of a child that lived sixteen days. After death it was found that the interauricular and interventricular septa were both defective; the aorta arose from the right ventricle, and the pulmonary artery (which for some distance was a solid cord) from the left; the right superior vena cava (formed by a vena azygos and the right brachio-cephalic vein) opened into the right auricle; the inferior vena cava and the left superior vena cava (formed by a vena azygos), the left brachio-cephalic vein, and the four pulmonary veins, united into a common stem, opened into the left auricle. The trachea, above the normal site of bifurcation, gave off, on the left side, a separate bronchus, which passed to the upper lobe of the three-lobed left lung. The right stem bronchus had a double eparterial bronchus. The spleen was absent, and there was an anomalous arrangement of the peritoneum in connection with the liver. Chiari's case represented an unusual form of trifurcation of the trachea; commonly there is simply premature origin of the normal eparterial bronchus to the right side (or to the left in transposition of the viscera).

I have already referred to cases of œsophageal occlusion in which the lower end of the œsophagus opened into the trachea (*vide* p. 463); but there are yet other malformations of the trachea and bronchi, including their *absence* (when the lungs are attached immediately to the larynx), congenital *narrowness* or *shortness* of the trachea or left bronchus, *defect* or *excessive number* of the tracheal rings, and congenital *dilatation* of a part of the trachea, or the presence of a *diverticulum.* Malformations of the pulmonary artery and veins have been described already.

Malformations of the Thymus Gland.

Carl Hennig, in Gerhardt's *Handbuch der Kinderkrankheiten* (Nachtrag iii. 1893), gives an interesting account of the malformations of the thymus gland. It may be absent in otherwise well-formed new-born infants, but more often in acephalic twin fœtuses;

it may be abnormally small or abnormally large; or it may show an increase in the number of gland lobes. Instances of absence were reported by H. Harrington (*Lond. Med. Gaz.*, iii. 314, 1828–29) and A. Clark (*Lancet*, ii. for 1896, p. 1077). In the dissection of all kinds of monstrous fœtuses I have been struck by the constancy of the thymus gland: in a specimen of deformed twin, paracephalus dipus acardiacus, it was absent (*Trans. Edinb. Obst. Soc.*, xviii. 48, 1893); but in other types of monstrosity I always found the thymus, although in some instances, such as exomphalos, it was somewhat abnormal in position. I believe, therefore, that this organ plays an important part in the physiology of the embryo and fœtus, although it is not as yet quite clear what its special duties are.

CHAPTER XXVII

Merosomatous Terata (*cont.*): Malformations of the Abdomen: Gastroschisis: History, Nomenclature, Classification, Clinical Characters, Morbid Anatomy, Teratogenesis, Literature; Hernia of the Umbilical Cord; Intestinal Diverticula; Intestinal Stenosis and Atresia; Hour-glass Stomach; Malposition of Intestines; Anomalies of Appendix Vermiformis; Congenital Hernia and Hydrocele; Anomalies of Liver and Gall Bladder; Anomalies of Spleen, Suprarenal Capsules, Pancreas, and Blood Vessels; Congenital Umbilical Neoplasms.

There can be no doubt as to which of the many malformations and monstrosities of the abdomen (gastro-terata) should be selected for special description: *gastroschisis* or defect of the abdominal walls with protrusion of the viscera suggests itself at once as the typical teratological state. It is relatively common, for out of 331 specimens and cases of antenatal morbid change examined by me I have met with sixteen examples of it, not including cases of hernia into the umbilical cord (of which there have been three); it is a striking malformation; and it raises practically all the questions concerned with the teratology of the abdomen. It is, therefore, eminently suitable for consideration as the type-monstrosity. Illustrations of specimens in my possession are given in Figs. 25, 26, 27, 28, 29, 30, 31, 34, 54, and 75.

Gastroschisis.

The *history* of gastroschisis (defective abdominal walls and exposed viscera) goes back to the time of Lycosthenes, who in his *Chronicon* (p. 596, 1557) reports the birth of a monstrous infant at the town of Ploa in Voitland (Plauen in Voigtland?); this infant, as may be learned from the description and the illustration which Lycosthenes gives, had its lower limbs bent up on the abdomen with the knees extended, had a curiously shaped high head ("ad similitudinem citharis," like a turban), and showed a sac, containing the intestines hanging from an opening in the chest and abdomen; this was in the year 1547. The illustration given in the *Chronicon* produces the impression of having been touched up for artistic effect, but there is no reason to doubt that it represents a real case of gastroschisis, the first of the long series of specimens with which the archives of teratology are now supplied. Other early instances were reported by N. Steno (*Acta med. et phil. Hafn.*, i. 200, 1673), L. Schroeck (*Miscell. Acad. nat. curios.*, Dec. i., Ann. vi.-vii. 341, 1677), G. A. Fried (*Diss. inaug.*, Argentorati, 1760), Preuss (*Acad. nat. curios. ephem.*, Cent. vii.-viii., Appendix, p. 117, 1719), E. Sandifort (*Acta Helvet.*, vii. 56, 1772), and M. Saxtorph (*Acta reg. Soc. med. Harn.*, i. 191, 1783). By the beginning of the nineteenth century the observations were sufficiently numerous to permit attempts at classification being made, and now at the beginning of the twentieth century there are so many cases of gastroschisis on record that the mere task of collecting all the references is arduous.

The *nomenclature* and *classification* of instances of gastroschisis require some words of explanation. "Exomphalos" which is sometimes used as a synonym of gastroschisis is not, in my opinion, so appropriate, for it concentrates attention too much upon the umbilicus, and, further, it has been to some extent appropriated for the cases in which there is an umbilical hernia in the ordinary sense of the word. In the earlier records no single name was given to the monstrosity, which was referred to by a descriptive phrase; thus Fried (*op. cit.*) entitled his communication "De fœtu intestinis plane nudis extra abdomen propendentibus nato." He subdivided all the cases into those in which the intestines were contained in a sac and those in which they were not. J. F. Meckel (*Handbuch der path. Anatomie*, i. 95, 117, 1812) gave the name of "partial fissure of the anterior surface of the body" to these monstrosities, and made some distinction between various specimens according to the region specially affected. C. Meyer in his dissertation ("De fissuris hominis mammaliumque congenitis," Berolini, 1835) used the name ventral fissure, and divided all such fissures into median and lateral and into complete and partial. A far more extensive scheme of classification and denomination was introduced soon after by Isidore G. Saint-Hilaire (*Histoire des anomalies*, ii. 264, 1836). He gave the name celosomus to the second tribe of the order of the autositic monstrosities; this tribe contained the single family of the celosomian terata, but it was subdivided into six genera. These six genera were arranged in two groups. In one there was eventration of both the abdominal and the thoracic viscera through an opening affecting both the abdomen and the thorax; here was placed the genus *celosomus* in the strict sense in which there was a lateral or median eventration with fissure, atrophy, and even total absence of the sternum and hernial displacement of the heart; here also was placed the genus *pleurosomus*, in which there was a lateral eventration affecting chiefly the upper part of the abdomen and extending to the chest-wall, with incomplete development of the arm of the same side. In the second group were four genera which all agreed in the fact that the eventration affected the abdomen alone and did not extend to the thorax: the first genus was called *aspalasomus*, in which there was a lateral or median eventration, affecting chiefly the lower part of the abdomen, and the urinary organs, the genitals, and the rectum opened externally by three distinct orifices; the second genus was *agenosomus*, in which, again, the eventration was lateral or median and affected the lower part of the abdomen, but the urino-genital organs were either absent or very rudimentary; the third genus was *cyllosomus*, in which the eventration was always lateral and chiefly affected the lower part of the abdomen, and there was absence or incomplete development of the lower limb of the same side; and the fourth genus was *schistosomus,* in which the whole abdomen was open either in the middle line or laterally, and the lower limbs were either absent or very imperfect. There are defects and complexities and overlapping in Saint-Hilaire's system, but it has been widely used, and I have therefore stated it fully; I do not, however, intend to employ it in this work, and I may consequently pass from the subject with one further reference to it. N. Joly in his *Mémoire sur un nouveau genre de monstres célosomiens,* Toulouse, 1848, and in an earlier article, added three new genera to the already existing six of Saint-Hilaire: to one he gave the name *dracontisomus,* because in it, in addition to a median eventration affecting the thorax and abdomen, the vertebral column was greatly twisted on itself, and the ribs ran outwards almost horizontally like the wings of a dragon or flying lizard (hence the name); the second he called *chelonisomus,* and in it the eventration was either median or lateral and abdomino-thoracic in extent, and the spine was so bent that the sacral region and lower limbs were turned backwards and enclosed within a sort of dorsal pseudo-thorax formed by the ribs bent backwards; to the third the term *streptosomus* was given, because in it the spine was so twisted that the lower limbs were displaced to right or left, and the eventration was again median and abdomino-thoracic in extent. The various genera of the Saint-Hilaire-Joly scheme are, therefore, as follow:—

Celosomus,
Pleurosomus,
Aspalasomus,
Agenosomus,
Cyllosomus,
Schistosomus,
Dracontisomus,
Chelonisomus,
Streptosomus.

I do not employ the above system in the present work because I have adopted the regional method of arrangement, and because I think that several of the names are confusing or at any rate have a meaning not immediately obvious. The fœtus may be like a dragon or a turtle, but the likeness is not so striking as to make the name anything less than an etymological puzzle. In Chapter XXV. I described fissure of the sternum with ectopia cordis and pleurosomus with protrusion of the lungs, and I touched upon chelonisomus on p. 313, so that these monstrosities do not now require to be dealt with. For these and other reasons I prefer to describe here only the teratological states which affect the abdominal region (the gastroterata); and, as I have said, Saint-Hilaire's nomenclature and classification do not adapt themselves to this plan.

Gurlt's name for gastroschisis was *schistocormus fissiventralis,* and Forster's was *fissura abdominalis* (*Die Missbildungen des Menschen,* p. 109, 1865); the latter author divided cases of fissura abdominalis into the complete form, into umbilical hernia, and into extroversion of the bladder, and under the first heading he subdivided the cases according to the region of the abdomen affected. Ahlfeld, however, pointed out that the defect rarely corresponded with any degree of accuracy to any anatomical region (*Die Missbildungen des Menschen*

p. 204, 1882); he separated off ordinary umbilical hernia and extroversion of the bladder and used ectopia viscerum as a synonym for fissura abdominalis. I think there is no doubt that it is a better plan to separate hernia of the umbilical cord and extroversion of the bladder from the ordinary cases of gastroschisis in which there is a greater or less defect of the anterior abdominal walls with protrusion of the abdominal viscera; I have adopted this method here. At the same time it has to be noted that Taruffi (*Storia della teratologia*, vii. 406, 1894) retains the idea of a regional classification and nomenclature, and arranges the specimens of gastroschisis in seven groups as follow:—

1. Epigastro-schisis: aperture in epigastric region.
2. Epi-omphalo-schisis: aperture in the epigastrium in continuation with the umbilicus.
3. Thoraco-omphalo-schisis: umbilical aperture continued into the sternum.
4. Hypogastro-schisis: aperture in hypogastrium.
5. Pleurosomato-schisis: lateral aperture of the trunk.
6. Hypogastro-etro-schisis: aperture of the hypogastric region, including the symphysis pubis.
7. Hologastro-etro-schisis: aperture of the whole abdomen, extending to the symphysis pubis.

I do not, as I have said, follow Taruffi in his arrangement; I prefer to describe extroversion of the bladder by itself, and to regard the other types as varieties of gastroschisis not sufficiently clearly marked off from each other as to deserve separate treatment. No system of classification is perfect, and it is, therefore, important to avoid complexity both in arrangement and terminology.

The *clinical history* of cases of gastroschisis differs in no important detail from that in anencephaly or other grave monstrosity. Postnatal life is usually very short: in one of my specimens, that represented in Figs. 27 and 28, the heart, which was outside the body, beat for fifteen minutes after birth; the mother, who was quite healthy herself, had previously given birth to four normal and healthy infants; there had been no maternal impression in pregnancy. In another case (Fig. 75) there was such marked hydramnios that the woman was thought to be suffering from an ovarian cyst; she was forty-one years of age and had had five previous pregnancies terminating in the birth of four living and one dead fœtus. The mother of another specimen of gastroschisis (Fig. 29) was healthy but suffered from great pain in the left iliac fossa towards the end of pregnancy; her husband was crippled with sciatica and was alcoholic. In 1891 I received from Dr. W. Paterson a very marked specimen of gastroschisis with fissure of the symphysis pubis, anencephaly, spina bifida, and retroflexion of the vertebral column; the mother was a primipara who during the third month of pregnancy got a bad fright from seeing a child narrowly escape being run over in the street; there was great hydramnios, the liquor amnii "gushing like a mill stream." In another case (Figs. 30, 31) the mother had great pain during pregnancy in one iliac fossa; this symptom was also present in A. R. Simpson's case (*Trans. Edinb. Obst. Soc.*, vii. 80, 1882).

The diagnosis of the monstrous state of the fœtus is usually made during labour; for there seems to be a special tendency for the protruding intestines and other abdominal viscera to form the presenting part, and the palpation of them is usually immediately helpful. A loop of bowel may be mistaken for a loop of the umbilical cord, but not if the presence of a mesentery in the former case be kept in mind. The tendency of the exposed intestines to present at the os uteri in labour is specially dwelt upon by A. R. Simpson in his article referred to above (*loc. cit.*); it is to be explained partly at least by the fact that the normal fœtal attitude of flexion is often replaced by one of extension, and that in consequence the fœtus is so folded that the narrow end of the ovoid is formed by the exomphalos. In this relation I may give some notes of the latest specimen of gastroschisis which I have been able to examine, one sent to me by Dr. Rorie of Cardenden in May 1904. The mother was a secundipara, twenty-four years of age; she fell in labour, and a midwife finding a sac presenting at the os ruptured it under the belief that it was the bag of membranes; on the following day Dr. Rorie was called in and found the fœtal liver and bowels protruding through a fully dilated os and giving the sensation as if there was a placenta prævia; there had been some hæmorrhage and the fœtus was firmly impacted, therefore version was accomplished and the monstrosity delivered. During version the liver and a piece of intestine were detached. Five months previously the mother had a fall while lifting a heavy chest and thought that "everything came away then." I need not multiply instances of this kind, but may add that the presentation is not invariably an abdominal one; sometimes the head is the lowest part, more especially when there is anencephaly, a not uncommon complication of gastroschisis. Labour often comes on prematurely, and there is usually delay until version is performed. There is generally some hæmorrhage in labour, for the placenta, being closely attached to the fœtus, is apt to be detached early from the uterine wall. The sac containing the abdominal viscera is generally ruptured at some time during delivery (Glanville Morris, *Trans. Edinb. Obst. Soc.*, xix. 103, 1894).

The *morbid anatomy* of gastroschisis is a matter of some complexity; I shall first describe certain characters which are fairly common to all the specimens, and thereafter deal with more exceptional details. The most obvious feature of the monstrosity is the absence of the anterior abdominal walls. There is no umbilical orifice, because there is absence of the abdominal wall in the region of the umbilicus. At the sides, and separated from each other by a considerable distance, are the margins of the ununited walls; they are usually continuous with the amniotic membrane, so that the abdominal viscera which protrude from the abdomen project into a sac formed by the amnion. There is consequently no properly formed umbilical cord, but vessels pass from the placenta to the fœtus in the walls of the sac formed by the amnion. These vessels are often much shorter than usual, and may consist of only one artery and one vein. The whole placenta is, therefore, situated much nearer to the fœtus than is normal, and has often been described as adherent to it (*vide* pp. 171–175). The intestines and other abdominal organs which lie in this sac may be surrounded by a second membrane, the parietal peritoneum (Fig. 75); but apparently this is wanting in most of the marked cases; perhaps it is not developed, or it may be fused with the amniotic sac itself. Sometimes the intestines are adherent to the walls of the sac by bands or threads.

The protruded viscera vary somewhat in different cases. The intestines are always present, but the rectum (when it exists) and a variable part of the descending colon remain in the abdominal cavity. The stomach may be partly outside the body and the liver wholly so (Fig. 75), or the liver, stomach, spleen, and even the heart and a lung may be all external to the abdomen (Figs. 27, 28). The kidneys and suprarenal capsules are usually intra-abdominal in position; but they may be drawn forward out of their place, and, on account of the dislocation of other organs, they form new relations with surrounding

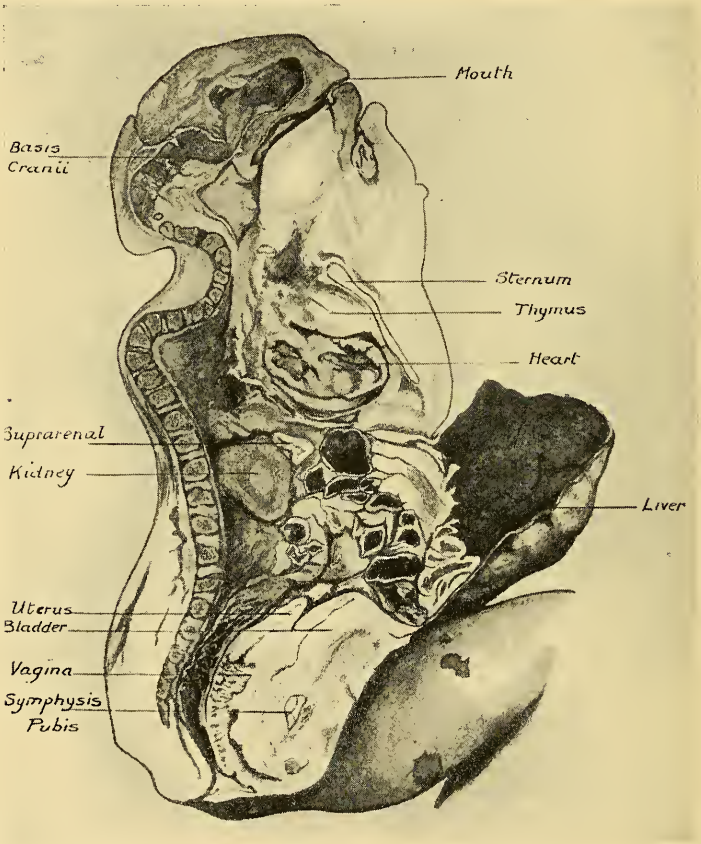


Fig. 75.—Sectional Appearances of Specimen of Anencephaly and Gastroschisis. Left slab of section shown. Specimen No. 29.

parts. The bladder may remain inside the abdomen (Fig. 75); but when the defect in the anterior abdominal wall extends so far down as to affect the symphysis pubis there may be not only displacement forward of the bladder, but also defective formation of its anterior wall (extroversion); in other cases the rectum and bladder may form a cloaca. It is not uncommon to find atresia ani; and the uterus (in the female) may be bicornate or entirely double (Thompson Lowne, *Catalogue*, No. 310, p. 85, 1893). The diaphragm is usually intact; but it may be wanting, when the heart may be among the extruded viscera. There may be various irregularities in the arrangement of the vessels: thus the aorta may be continuous with a single artery passing to the placenta (in T. H. Bryce's case, reported in the *Journ. Anat. and Physiol.*, xxix. p. 553, 1895, it was the right umbilical artery that formed this continuation); in one of A. Rischpler's specimens (*Arch. f. Entwcklngsmechn. d. Organ.*, vi. 556, 1898) there was persistence of the right umbilical vein with the presence of only one artery; and in another case the umbilical vein did not enter the liver, there was no ductus venosus, and the inferior vena cava and the superior mesenteric artery were absent.

It is very common to find retroflexion of the spinal column and absence of certain of the vertebræ. There were only thirty vertebral bodies in one of my specimens (Fig. 75), and the number was still further reduced in others. The spinal retroflexion, which may be combined with torsion, is often very remarkable. Thus, in one of my cases (Fig. 28), there was an extraordinary sigmoid curve, a very prominent cervico-dorsal lordosis being compensated by an equally prominent dorso-lumbar cyphosis; in another (Fig. 75) the curves were similar but less marked; and in some other specimens (Nos. 28 and 331 in my collection) the retroflexion was so excessive that the pelvis could easily be made to touch the back of the head. This state of the spine may perhaps be regarded as a persistence of what is normal at the third week of antenatal life (*vide* Fig. 12, p. 34); but the curves do not always coincide. Backward displacement of the lower limbs may accompany this spinal deformity, and they may be found lying posteriorly, a teratological fact which may give rise to a clinical mystification during the operation of version; the limbs may also be rotated (L. Kriwsky, *Monatschr. f. Geburtsh. u. Gynaek.*, xi. 895, 1900), somewhat as they are in sympodia, but without being fused together. There may likewise be spina bifida and anencephaly, although these are rather of the nature of accidental complications of gastroschisis than of associated anomalies; the same remark applies to malformations of the upper extremities such as club-hand (Thompson Lowne, *Catalogue*, No. 308, p. 84, 1893).

The teratological characters which have been described are met with to some extent in all cases of gastroschisis; but there are others, to which I now direct the reader's attention, that are less constant. Some specimens, for instance, show an opening in the anterior abdominal wall situated in the epigastric region and limited to it; in most of them, however, the opening permits the protrusion of the heart, with or without its pericardial sac, and accompanied by defect of the diaphragm; these, therefore, are rather to be reckoned with the cases of sternoschisis and of ectopia cordis than with gastroschisis and ectopia intestinorum. There are, however, a few cases in which there seems to have been protrusion of *abdominal* contents through an epigastric opening, and among these Mr. James Calder's record is quite definite (*Med. Essays and Observ.*, Edinburgh, i. 203, 1733). He wrote, "I was sent for to visit a new-born child that had a large Share of its Intestines lying without the Teguments of the *Abdomen*; I at first imagined the containing Parts had been torn in the Birth, but upon Examination found the Navel intire, and a Perforation half an Inch above it, thro' which the Guts had fallen out, with the Skin closely united to them. The Child seem'd otherwise to be as lively and Brisk as any new-born Infant uses to be, and for 12 or 14 Hours it received Milk and Syrups by the Mouth, without any Appearance of Uneasiness; but after that time it vomited every thing till its Death, which happened four Days after, and all the while it had no Passage by the *Anus*." At the autopsy it was found that the protruded intestines consisted of the jejunum, ileum, and part of the colon and cæcum. "The Mother could not remember ever to have been surprised, frighted, or hurt during all the Nine Months of her going with Child." Probably epigastric gastroschisis is the rarest of all the varieties of this monstrosity.

Less rare are the cases in which an opening exists in the epigastrium, extending down to and including the umbilicus, and permitting the exit of some of the abdominal contents. Taruffi (*op. cit.*, vii. 413, 1894) has collected eight instances, including one by G. Tonelli (*Ann. univ. di med.*, lxxxii. 441, 1837) and one by himself. In the latter case the skin of the abdomen under the ensiform cartilage and ribs was wanting, and its place was taken by an amniotic sac containing the heart, stomach, small and large intestine, and the right kidney; the rectum and anus were absent.

It is more common to find an abdominal opening such as that described above continued upwards into a thoracic defect and associated with fissure of the sternum. I have already written of such cases in Chapter XXV. under the heading of sterno-epigastric ectopia cordis; but they really belong rather to this chapter, for although they may be regarded as connecting links between thoracic and abdominal fissures they are rather to be looked upon as instances of gastroschisis complicated or associated with sternoschisis. They have the characters which I have described as common to gastroschisis, and need not, therefore, be again referred to here.

A more exceptional arrangement is that in which coils of intestine protrude through an opening in the hypogastric region, often small in size, and not including the umbilicus. In J. G. Hasenest's observation ("Fœtus mostrosi ex imaginatione deturpati," *Acta Acad. nat. curios.*, vi. 31, 1742), the gastroschisis was accompanied by marked torsion of the spine and absence of one lower limb. G. A. Fried's case (*op. cit.*) seems to belong to this rare variety. The urinary bladder is intact, and the urachus may be seen traversing the abdominal wall at the side of the opening to reach the umbilical cord; these characters serve to mark off this exceptional type from the ordinary forms in which there is hypogastric eventration with extroversion of the bladder.

Somewhat exceptional, also, are the cases of lateral opening in the abdomen with eventration (pleurogastroschisis). I have met with a case of this kind in which the fissure, however, was not restricted to the abdomen, but extended also to the thorax (Fig. 34, p. 181); in this instance the arm of the affected side was deformed and fixed by the wrist to the margin of the opening by a band of skin. In another case which I saw with Dr. D. Milligan in 1897 (No. 199 in my list) there was a defect in the abdominal wall in the left side of the abdomen through which the abdominal viscera protruded, but the skin was continuous and, therefore, the condition was rather to be regarded as one of lateral hernia than of gastroschisis; the infant, a male, also exhibited lumbar spina bifida (ruptured during birth) and deformities of the lower limbs; he survived his birth for several weeks. A more typical instance was reported by A. Bertino (*Ann. di ostet. e ginec.*, xxi. 735, 1899): it was a male fœtus, normal in all its parts save in the abdominal region; there was an opening in the right half of the anterior abdominal wall, about the level of the umbilicus, through which a packet of abdominal viscera (with no membranous covering) projected; the opening was nearly circular, had a diameter of 4 cm., and was separated from the normally closed umbilical ring by a tract of normally constituted abdominal wall; the extruded mass was made up of three lobes, an upper (consisting of the lower end of the œsophagus, the stomach, and duodenum), a middle (made up of small intestines adhering together by pseudo-membranes), and a lower (constituted by cæcum, ascending colon, transverse colon, and descending colon as low as the sigmoid flexure); and the umbilical cord had its normal appearance, and contained the usual three vessels, the vein passing in the superficial part of the wall skirting the margin of the opening through which it passed to be distributed normally to the liver. When the lateral opening is lower down, as in a specimen which Dr. F. W. N. Haultain allowed me to examine, and which is represented in Fig. 76, the lower limb of the affected side may be absent (cyllosomus). A similar case was reported by H. Stern (*Diss. inaug.*, Königsberg i. Pr., 1896); and in A. Brabandt's specimen (*Diss. inaug.*, Leipzig, 1896) both the right os innominatum and the leg were absent. Schaefer (*Diss. inaug.*, Bonnæ, 1837) and W. Vrolik (*Tabulæ ad illustrandam embryogenesin*, Plate lxiii. Fig. 4, Plate lxiv. Figs. 4, 5, 1894) gave good descriptions of this condition (gastroschisis and monopodia); and Taruffi (*op. cit.*, vii. 549, 1894) has included these cases with the one-legged fœtuses in which there was no gastroschisis in the group which he calls *mono-anileus apus* (absence of one os innominatum and corresponding lower limb).

Gastroschisis occurs in the lower animals as well as in the human subject: it has been observed with comparative frequency in the calf, but has also been noted in the pig, the lamb, the kitten, and in reptiles and birds.

The *teratogenesis* of gastroschisis, as was to be expected, has given rise to much discussion. The amniotic theory has been already discussed in this volume (pp. 168–175), and I need not again open up the whole subject. There have been many theories, including those of shortness of the umbilical cord, injury to the fœtal abdomen, adhesions of the amnion, twisting of the vertebral column, smallness of the thoracic and abdominal cavities, and simple arrest of closure of the anterior abdominal walls; the great difficulty consists in separating the causes from the effects, for, obviously, a small abdominal cavity may either be the cause or the result of the eventration. In order to account for the frequent association of defects in the terminal part of the bowel and in the generative organs, T. H. Bryce (*Journ. Anat. and Physiol.*, xxix. 553, 1895) brings forward defective development of the allantoic stalk and hind gut which interferes with the incurving of the tail end of the embryo and maintains the attitude of retroflexion of the trunk. This is a matter upon which investigations into the vascular supply of the fœtus and placenta may throw some light; for if it can be shown that the placental blood supply is furnished by vitelline and not by allantoic

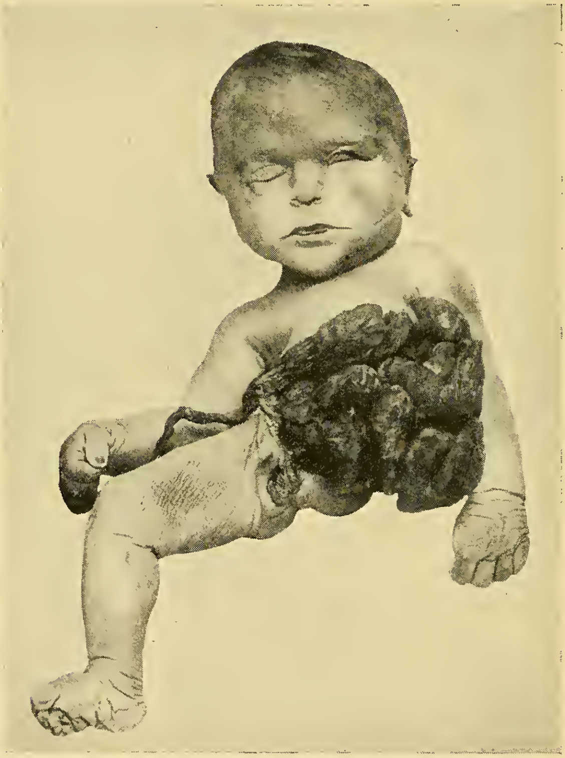


Fig. 76.—Specimen showing Absence of Left Lower Limb with Protrusion of Viscera (Cyllosomus).

vessels, it would give some support to the idea that the allantois was defective.

Literature.—There is a large literature bearing on this subject. The references, however, are scattered, and little care has been taken in lists and catalogues to separate records of true gastroschisis from cases of hernia of the umbilical cord and ring. For instance, in the *Index Catalogue* (Washington), some references to gastroschisis appear in vol. ix. under the heading MONSTERS, *from defect or malformation of abdomen and thorax*; others come under ABDOMEN, *abnormities of* (vol. i. 5, 1880; 2 s., i. 7, 1896); and yet others under HERNIA, *umbilical* (vol. vi. 168, 1886; 2 s., vol. vii. 60, 1902). Taruffi (*op. cit.*, vii. 403–430, 492–507, 1894; viii. 561–563, 1894) makes an attempt, with some measure of success, to separate gastroschisis both from umbilical hernia and from hernia of the umbilical cord. I refer my readers to these bibliographical sources, and simply add here a few references that I have found useful: J. Lindsay, *Trans. Glasgow Obstet. and Gynæc. Soc.*, iii. 233, 1903; Leith Napier, *Trans. Obstet. Soc. Lond.*, xxxvi. 302, 1895; A. Klautsch, *Centrlbl. f. allg. Path. u. path. Anat.*, vi. 385, 1895; H. M. MacGill, *Lancet*, ii. for 1894, p. 687; P. Ardouin et E. Kirmisson, *Rev. d'orthop.*, viii. 104, 1897; H. Lockwood and C. Addison, *Quart. Med. Journ.*, vii. 231, 1899; E. Stangl, *Arch. f. klin. Chir.*, lxxiii. 853, 1904; L. E. Deshusses, *Thèse*, Lille, 1903.

Congenital Umbilical Hernia.

Much more common than gastroschisis is the condition known as *congenital umbilical hernia*, omphalocele ab ortu (Plater), or schistocormus exomphalus (Gurlt). It is essentially a herniation of some of the abdominal contents into the umbilical cord, a *hernia funiculi umbilicalis*; and, like many other malformations, represents a condition which is normal in early antenatal life, but if persistent becomes obviously teratological. By some writers it is made to include hernias through the umbilical ring which come on soon after birth (*e.g.* at the fall of the cord); but such states, although they may be predisposed to antenatally, are really postnatal developments in the great majority of cases; I do not, therefore, specially consider them here, although I freely admit that antenatal influences take their place along with delayed and incomplete closure of the umbilical ring, increased abdominal pressure, and the like, in their causation. There is, with all possible care in classification, a certain degree of confusion existing regarding the cases in which the hernia occurs into the cord and those in which it is truly umbilical; for it is quite possible that in later fœtal life, after the intestine has been withdrawn from the root of the cord and retracted within the abdomen, a hernia may occur through the ring closely resembling that which develops during the early weeks of postnatal life, but differing in the fact that the umbilical cord arises from it. In this work, however, I deal rather with the truly antenatal and embryonic malformations, those which arise during the embryonic phases of development; on that account it is with hernia funiculi umbilicalis that I am specially concerned.

Hernia of the umbilical cord is comparatively common; it is not indeed seen so often as hare-lip, cleft palate, spina bifida, or anencephaly, but it occurs about once in five thousand births (O. Lindfors, *Nord. med. Ark.*, xv. No. 25, 1–34, 1883). In 331 cases of antenatal disease and deformity examined by myself, there were four cases (Nos. 27, 39, 185, and 198 in my list) of hernia into the cord; and Taruffi (*op. cit.*, vii. 365; viii. 413, 1894) has gathered together from medical literature 130 cases, without completely exhausting the list.

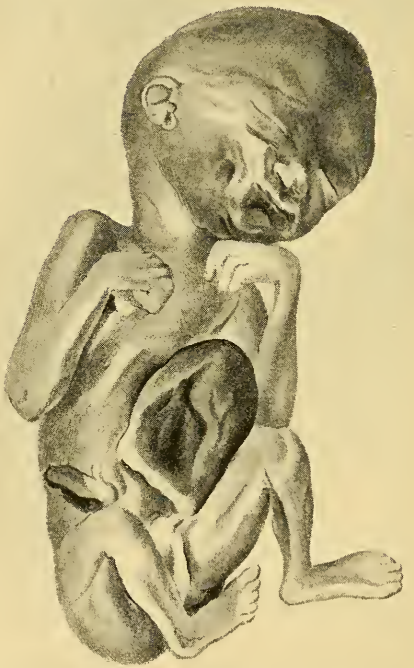


Fig. 77.—Case of Hernia of the Umbilical Cord.
Specimen No. 27.

The *clinical history* of hernia funiculi umbilicalis seldom contains any antenatal indications, with the possible exception of those of hydramnios. In one of my specimens (Fig. 77) the mother had a record of habitual abortions; she had been ten times pregnant, but had carried only three children to the full term; she had generally aborted about mid-term, and the fœtus with umbilical hernia (Fig. 77) was regarded as at four and a half months; there was a large quantity of greyish-brown liquor amnii; and the fœtus, which was alive when born, made lively movements for about five minutes (*Trans. Edinb. Obstet. Soc.*, xvii. 241, 1892). In the above case the placenta seemed healthy; but in another one (*Trans. Edinb. Obstet. Soc.*, xvii. 243, 1892), in which the fœtus was born with the membranes unbroken, the placenta showed lesions regarded as syphilitic. In both these cases delivery took place at mid-term; but in that of an infant (No. 185) sent by Dr. Waddell of Slamannan into the Sick Children's Hospital, Edinburgh, in 1896, the labour was at the full time and was accompanied by marked hydramnios; in this instance (which I examined with Dr. Joseph Bell) the mother's health and heredity had been good, but on the father's side there was a very clear history of scrofula (*Trans. Edinb. Obstet. Soc.*, xxii. 27, 1897). In a case which I examined with one of my dispensary pupils (Mr. Dick) in 1897, the infant was the product of a second pregnancy, and the elder child was quite normal. (Case No. 198.) Sometimes the umbilical hernia is the presenting part in labour (as in the case of the fœtus shown in Fig. 77); at other times the head presents, and there is delay with the birth of the trunk on account of the large size of the abdomen (as in Dr. Waddell's case). Male infants are more often affected with hernia of the cord than females; G. Buschan (*Diss. inaug.*, Breslau, 1887) gives the proportion as 43 males to 26 females.

The clinical history after birth has a sad similarity, for most of the infants perish in a few hours or days, unless they are skilfully operated upon. The cause of death is commonly rupture, mortification, or inflammation and suppuration of the sac, with peritonitis; and sometimes there is strangulation of the hernia. The result, however, is not invariably fatal; for retreat of the protruded parts into the abdomen and cicatrisation may occasionally occur (*e.g.* in the cases of L. Margariteau, *Bull. gén. de Thérap.*, xlviii. 544, 1855, and Stoltz, *ibid.*, liii. 467, 1857), and treatment by operation or by methodical compression has sometimes succeeded. Details of the probable mode of spontaneous cure, and of the various plans of treatment, are given by E. Kirmisson (*Traité des maladies chirurgicales d'origine congénitale*, pp. 230–233, 1898). The great difficulty which meets the operator is the fact that the abdominal cavity is not large enough easily to contain all the viscera when the protruded parts are replaced. At the same time, the surgery of to-day has greatly improved the prognosis in all these cases.

In its *morbid anatomy* hernia of the umbilical cord presents fairly constant characters. In the umbilical region of the abdomen there is seen a more or less spherical projection, varying in size from that of a walnut to that of the closed fist, or even of the fœtal head. It is easy to recognise that the swelling is funic in nature, for the distal part of the cord may arise from it and pass to the placenta, or there may be an indication of the umbilical ring between its base and the abdominal wall. Sometimes the sac is defective or absent, and the viscera are exposed: this occurs most often when there is no true cord, when the sac is simply composed of amniotic membrane passing to the placenta, and when in consequence the birth of the child can hardly take place without rupture. In one of my specimens, however (that numbered 39, and given me by Dr. W. Fordyce), on account of the birth of the fœtus in the membranes this sac was found unruptured, lying between the infant and the fœtal surface of the placenta. Possibly, also, the sac may rupture in utero before the commencement of labour. In most cases, however, there is a sac which can be recognised as consisting of the sheath of the cord. At first it is smooth and transparent, and allows the contents of the hernia (intestinal coils and liver) to be seen plainly through it, but in a few days after birth it becomes opaque (inflammatory changes). Sometimes two membranes make up the sac-wall, and the inner of these is to be regarded as parietal peritoneum; but this is not a constant arrangement, and it is possible that the single membrane, when it is found, represents both the covering of the cord and the peritoneum, in an undifferentiated state. Generally there is a sharp line of demarcation at the umbilicus where the normal skin of the abdomen begins and the covering of the sac ceases; but the sac-wall may be, as it were, prolonged beyond the margin of the umbilical ring and only fade away gradually into the surrounding cutaneous covering.

It has been said that the herniated mass is generally round in shape; but it may, on occasions, be conical, and may even, in rare cases, show projections or diverticula (A. G. Luecke, *Diss. inaug.*, Halis Sax., 1854). It gets larger during straining or crying of the infant. Its relations to the vessels of the umbilical cord have not always been clear; at any rate they have not often been clearly described. A. Scarpa, however, in his monumental work (*Sull'ernie*, Pavia, 1819), has given details on this point, and has shown how one of the umbilical arteries may be absent; subsequent writers confirmed Scarpa's conclusions in the main. The umbilical cord, when it is clearly marked off, may arise either under or above the hernia, in the middle line or to one or other side. From the descriptions given it seems to me to be quite likely that the vessels in the cord which run to the abdomen (especially when they consist of only one artery and a vein) are really vitelline (omphalo-mesenteric) and not umbilical (allantoic) in nature.

The contents of the hernial sac vary somewhat, but not to the extent that they do in gastroschisis. Most often the intestines are met with, and the ileum is very constantly present; the large intestine is less frequent. Next in frequency among the extruded viscera is the liver, and there are also a few cases in which this organ formed the sole contents of the sac (J. B. Palletta, *Exercitationes pathologicæ*, pt. 1, Art. x. p. 161, 1820); the stomach also may be found; and among the rarer structures may be named the spleen, the pancreas, a kidney, and even the heart (in cases of defect of the diaphragm). When the liver is either the only or the most obvious organ in the sac the name *hepatomphalocele* has sometimes been given to the condition. This organ may lie partly within and partly outside the abdomen, and it may show so deep a constriction at the umbilical ring as to suggest that it consists of two parts or that there is a "double liver." It is an interesting question whether the malformation of the liver in these cases is due to the hernia or is the cause of it. In R. C. Buist's specimen (*Trans. Edinb. Obstet. Soc.*, xxii. 25, 1897), which I had an opportunity of examining, the projecting mass of liver substance grew from the quadrate lobe; this supernumerary structure may have prevented the normal closure of the umbilical ring, or it may have resulted from displacement of the liver through it, by traction upon the umbilical vein passing into the hepatic substance. The question, however, cannot be settled without a more thorough knowledge of all the determining factors that have to do with the closure of the anterior abdominal wall in embryonic life. Some very interesting speculations have been made regarding lowering of the level of the diaphragm, shortness of the umbilical vein, and the relation of the umbilical vessels to the duodenum; but they are only speculations. The contents of the sac may show adhesions to the sac-wall and to each other; when there are no adhesions the organs may to some extent be returned to the abdominal cavity.

Associated malformations are not uncommon in connection with hernia of the umbilical cord. There may, for instance, be anencephaly, spina bifida, club-feet, club-hands, atresia ani, ectopia vesicæ, and retroflexion of the spine. As might be expected, the associated intestinal malformations are of great interest, and demand for their full elucidation a knowledge of the ontogenesis of the lower end of the alimentary canal such as we do not at present possess. There may, for instance, be varying degrees of defect of the lower bowel, such as atresia ani and atresia recti; the whole of the large intestine may be wanting and the small intestine may end at an opening in the wall of the hernial sac, possibly but not certainly produced by antenatal inflammation and ulceration (A. Billi, *Ann. univ. di med.*, clxxvii. 492, 1861); or, again, the lower end of the intestine may open in or near the ectopic bladder (P. Bockenheimer, *Arch. f. klin. Chir.*, lxix. 669, 1903). Meckel's diverticulum may be present in an umbilical cord hernia (*e.g.* in M. Wollstein's case, *Arch. Pediat.*, xxi. 416, 1904). The pelvic organs, also, may show malformations: there may be a splitting of the genital tubercle into two (P. Bockenheimer, *loc. cit.*), or the uterus may be bicornate or didelphic (J. H. Raymond, *Med. Rec.*, l. 514, 1896). Rarer anomalies are sacral tumour (A. Fleischmann, *Diss. inaug.*, Königsberg i. Pr., 1894), facial fissure (W. Jacobs, *Diss. inaug.*, Marburg, 1884), hydrocephalus (R. Lange, *Diss. inaug.*, Königsberg, 1891), multiple cysts of the umbilical cord (W. F. Boggess, *Arch. Pediat.*, xv. 678, 1898), polydactyly (Ponty, *Bull. Soc. d'anat. et physiol. de Bordeaux*, xv. 113, 1894), and persistence of cardinal vein and absence of ductus venosus (V. V. Preobrazhenski, *Journ. akush. i jensk. boliez.*, St. Petersburg, xiv. 141, 271, 1900).

In its *teratogenesis*, hernia of the umbilical cord illustrates very clearly the leading teratogenetic theories which have already been discussed in earlier chapters (*vide* pp. 129–224). There was, first, the theory of pressure or mechanical action, showing itself in external violence to the mother during pregnancy, in backward flexion of the spine of the fœtus, in shortness, essential or acquired, of the umbilical cord, and in overfilling of the abdomen with enlarged organs (*e.g.* kidneys) preventing the drawing in of the coils of intestine at the umbilicus. There was, second, the doctrine of disease as the cause of hernia funiculi umbilicalis, which practically took always the form of fœtal peritonitis and its effects; for instance, adhesions forming between the coils of intestine and the sheath of the cord might prevent the normal withdrawal of these coils into the abdominal cavity. Finally, there was the embryological theory, the hypothesis of arrested development or disordered ontogenesis. This view has taken many forms, and the changes have been greatly due to the gradual progress of our knowledge of the mode of development of the abdominal cavity and its contents. It seemed at first that nothing needed to be added to the statement that at an early stage in embryonic life there existed a physiological hernia funiculi, and that, therefore, the monstrosity was simply a persistence of this normally transitory phase. But difficulties arose when it began to be realised that it was not known in what manner the intestinal coils in the cord were drawn back again into the abdomen, and that, therefore, the cause of the non-withdrawal of them in teratological cases remained equally obscure. It was hazarded as an explanation that shortening of the mesentery might be the indrawing force, and that, therefore, non-occurrence of the shortening might lead to the persistence of the herniation. It was also suggested, and with more probability, that persistent traction on the intestines by the vitelline duct might be the cause of the malformation (a theory with which Ahlfeld's name has been specially associated, *Arch. f. Gynack.*, xi. 85, 1877); but there are difficulties in the way of a full acceptance of this theory, including the position of attachment of the cord to the herniated mass (*e.g.* lateral or inferior). At the present time there is a tendency to combine these various theories together in order to obtain a good working hypothesis to explain the different arrangements of parts which have been recorded. Narrowness of the amnion, a mechanical cause, has been invoked in order to explain the non-union of the margins of the umbilical ring (an arrest in development); and there have been many other more or less ingenious suggestions. The general conclusion to be drawn is that the explanation of hernia of the cord is to be found in embryology, but that all the details of the mode of origin can only be known when all the steps in the development of the abdomen and its organs are understood. Possibly, cases in which the herniation of the abdominal contents occurs laterally and not in the immediate neighbourhood of the umbilicus may throw light upon the whole subject. Such cases are rare, but not unknown. We have also to bring together the knowledge which has been gained regarding gastroschisis both median and lateral, for I believe that the causes operating in hernia of the cord and in gastroschisis differ not so much in nature as in the time in embryonic life when they come into play.

Intestinal Malformations—Diverticula.

Among the many anomalies found in the organs that lie within the abdomen, *intestinal diverticula* take a foremost place. Unlike gastroschisis and hernia funiculi umbilicalis, they are not visible externally and only come under notice when they establish a communication with the exterior (fæcal fistula at umbilicus, etc.) or interfere with the normal functions of the bowel and call for surgical interference. They come, therefore, under the heading of anomalies causing pathological manifestations in postnatal and not as a rule in antenatal life; they constitute very striking instances of the postponed effect of antenatal malformations. Since I have taken gastroschisis and hernia of the cord as the type-monstrosities of the region of the abdomen I shall only touch upon the anomalies now under consideration; but the reader who desires further details and more minute particulars will find them in Taruffi's work (*Storia della teratologia,* vii. 289–330, 1894), where forty pages are occupied with the discussion of them and with an enumeration of the bibliographical references to them.

As a matter of fact no part of the alimentary canal is exempt from diverticula. They may occur in connection with the œsophagus, and a few cases have been recorded in connection with the stomach. These gastric diverticula would seem to have been connected with the pyloric end of the stomach and have usually been observed only when they established an opening at the umbilicus; it is probable that the diverticulum is in the root of the cord at birth, and that, when the cord falls off, an opening is thus formed putting the gastric cavity in communication with the exterior (a gastric fistula). A probable instance was reported by H. Tillmanns (*Deutsche Ztschr. f. Chir.*, xviii. 161, 1882–83); in it the diverticulum formed a tumour, the size of a nut, at the umbilicus, and had the structure of the pyloric part of the stomach.

Duodenal diverticula have also been noted, although they are of considerable rarity. M. Roth (*Arch. f. path. Anat.*, lvi. 197, 1872) met with five cases; and other observers have reported examples, Taruffi, for instance (*op. cit.*, vii. 307), having in his museum a specimen showing two diverticula arising from the middle third of the duodenum. Gandy (*Bull. Soc. anat. de Paris,* lxxv. 691, 1900) has met with a case on the left side below the head of the pancreas; and Letulle (*Presse méd.*, Paris, i. for 1899, 13) deals with the subject of the "peri-vaterian" diverticula. From the jejunum, also, projections or appendages may arise: L. Ciniselli (*Sopra il gabinetto anatomo-pathologico esistente nello Spedale Maggiore di Cremona,* p. 54, 1869) has reported a case in which six of these took origin close together, while a seventh and a larger one was situated about 5 inches away from them. It is not clear, however, that Ciniselli's case had an antenatal origin. More recently, F. Buzzi (*Arch. f. path. Anat.*, c. 357, 1885) has described a "congenital" example of a jejunal diverticulum.

Diverticula of the large intestine also are somewhat rare; and when they occur it is not always possible to assume that they are congenital in origin. G. Fleischmann (*Leichenöffnungen*, 28, 1815), however, saw a case, affecting the colon, in a seven-months fœtus; and several probable instances have been recorded by more recent writers (G. Durante, *Bull. Soc. anat. de Paris*, lxxi. 318, 1896; L. Schreiber, *Deutsches Arch. f. klin. Med.*, lxxiv. 122, 1902; I. Tonta, *Verhandl. d. Gesellsch. deutsch. Naturf. u. Aerzte*, lxxi., pt. 2, 2 Hefte, 132, 1900). The nature of the so-called diverticula of the sigmoid flexure is not clear (G. P. Biggs, *Proc. N.Y. Path. Soc.* (1894), p. 44, 1895).

The most frequent site for intestinal diverticula is undoubtedly the ileum; and since the time when J. F. Meckel (*Handbuch der path. Anatomie*, i. 553–597, 1812) threw a flood of light upon the nature of this diverticulum by showing that it was the persistent vitelline or omphalo-mesenteric duct, no anomaly has been more thoroughly investigated and reported upon. The literature of the subject is very large, as may be learned by consulting the *Index Catalogue* (vol. vii. p. 27, 1886; 2 s., vol. viii. p. 233, 1903). The names most commonly given to these diverticula are *Meckel's diverticulum* (*diverticulum Meckelii*), *persistent omphalo-mesenteric duct*, and *persistent vitelline duct*. In form the diverticulum is tubular, very rarely conical, spherical, or pear-shaped; it is always narrower than the ileum from which it takes origin; and is always single, the rare cases of multiple diverticula arising from the ileum being in all probability of another nature altogether. It is attached to the intestine at one point or another in a portion of the ileum called the segment of Meckel; this segment is situated (in the fœtus) about 10 inches (25 cm.) above the ileo-cæcal valve, and measures a few inches in length; it is most exceptional to find the diverticulum taking origin below or above Meckel's segment. Its walls are continuous with those of the ileum; and its lumen may communicate freely with that of the bowel, or (rarely) may have a valve, or (more rarely) may be shut off from it entirely, when, of course, it will consist of an appendage blind at both ends. It comes off from the intestine generally on the side furthest away from the attachment of the mesentery, and at a right angle; but sometimes it may be situated laterally or even near the mesenteric attachment, and be directed obliquely. Rarely it possesses a mesentery of its own; very rarely it lies between the folds of the mesentery. In structure it is made up of all the layers of the normal ileum; it possesses Lieberkühn's follicles and may show a Peyer's patch, but the glands and villi are often rather poorly developed; the muscular coat may be deficient at the free end and allow the mucosa to form a hernial protrusion there which gives the diverticulum a peculiar clubbed or hammer-like shape. On its walls traces of the vitelline or omphalo-mesenteric vessels may occasionally be recognised.

The outer end of a Meckel's diverticulum may either float free in the peritoneal cavity or be attached. In the former case it may either end in a rounded extremity, in a swelling, or in one or more solid cords or threads; in an extraordinary case reported by E.

Neumann (*Arch. f. Heilk.*, xi. 200, 1870) it ended in a gland, the size of a pea, with the structure of the pancreas. Freely floating diverticula may endanger the postnatal life of the individual by forming loops round coils of intestine and leading to strangulation; they may also come to lie, alone or with a loop of intestine, in the sac of an inguinal (L. Hendee, *Beitr. z. klin. Chir.*, xxiv. 542, 1904) or umbilical hernia, or they may protrude into a hernia of the umbilical cord. When, on the other hand, the outer end of the diverticulum is fixed new possibilities arise. It may become attached to a coil of intestine and so produce obstruction and strangulation in one or other of the many ways described so clearly by F. Treves (*Intestinal Obstruction*, 37, 1884). This it certainly may do in postnatal life; and it is possible that it may also affect the bowel in a similar way in antenatal life, although then the results will differ on account of the comparatively quiescent state of the alimentary tract before birth. It is a reasonable hypothesis to think that in this manner some of the cases of congenital defect of the intestines may be produced. In other cases the diverticulum acquires adhesions with the umbilical ring: it may then be attached to the umbilicus or may even pass for a short distance into the cord; the diverticulum may remain pervious or may be changed into a more or less fibrous cord with traces of the vitelline vessels in it. Very often, however, the distal end of the diverticle opens at the umbilicus and forms a fæcal umbilical fistula or umbilical anus; in most cases this is probably the result of postnatal changes occurring at or about the time of the fall of the cord. (The literature of the subject is extensive and will be found in the *Index Catalogue*, vol. iv. pp. 1004, 1018, 1883; 2 s., vol. v. pp. 831, 837, 1900.) If the posterior end of the intestine be pervious the umbilical anus may gradually close; at other times it remains open and continues to discharge fæces and even lumbricoid worms; at yet other times, a small tumour, consisting of a prolapsed part of the mucous membrane of the diverticulum (vitelline prolapse), may form, and being cylindrical in shape may be described on superficial examination as a "penis at the umbilicus." Inflammation of the diverticulum ("diverticulitis") may develop in postnatal life (L. Picqué et A. Guillemot, *Bull. méd.*, Paris, xiii. 517, 1899), or a sarcoma may be found in it (O. Fried, *Diss. inaug.*, Erlangen, 1902).

Associated malformations are common in instances of intestinal diverticula, and may take the form of anencephaly, displacement of the viscera, acephaly (in the omphalo-angiopagous twin), thoracopagous double monster, and many other teratological states. Diverticula may also be met with in the lower animals (horse, dog, pig, lamb, calf); and are not restricted to the mammalia, but occur in birds as well.

The teratogenesis of Meckel's diverticulum presents no great difficulty. It is obviously a persistence of the transitory vitelline duct, and its frequent attachment to the umbilicus is easily explicable by embryology. Diverticula arising from other parts of the intestine than the segment of Meckel in the ileum admit of no such simple explanation; they might be regarded as distension-diverticula originating after birth, but in some cases at least they would seem to be indubitably antenatal.

Intestinal Stenosis and Atresia.

Antenatal narrowing or occlusion of the intestines is not very rare, but, being an internal malformation, doubtless often escapes discovery. I have already (Vol. I. p. 365) described the blocking of the pylorus which may cause symptoms and end in death a few weeks after birth, and need not refer to it again here, save to remark that it is probably the result of a fœtal rather than of an embryonic morbid state.

Obstruction of the duodenum has been noted, and I had an opportunity, in 1897, of examining a case of probable antenatal constriction of this part of the intestines at the point of entrance of the bile ducts (Case No. 190 in my list). There may also be a completely imperforate state of the duodenum causing the death of the infant a few days after birth. Then the upper half of the duodenum may be found greatly dilated and a transverse septum may exist just below. I have elsewhere (*Trans. Edinb. Obstet. Soc.*, xvii. 133, 1892) referred to a case of this kind which occurred in the hospital practice of the late Dr. Angus Macdonald: there was no communication between the first and second portions of the duodenum; the infant, a full-time male, developed jaundice, vomited constantly, and died on the sixth day after birth (*Trans. Edinb. Obstet. Soc.*, x. 229, 1885). Durante (*Bull. Soc. anat. de Paris*, lxxvi. 593, 1901) has recorded two cases of occlusion of the duodenum just below the place of entry of the bile and pancreatic ducts. Other duodenal cases have been reported by J. B. S. Jackson (*Boston Med. and Surg. Journ.*, lix. 355, 1858–59), L. Cordes (*Arch. Pediat.*, xviii. 401, 1901), C. Hess (*Deutsche med. Wchnschr.*, xxiii. 218, 1897), F. Heymann (*Monatschr. f. Geburtsh. u. Gynaek.*, x. 186, 1899), A. Katz (*Bull. Soc. anat. de Paris*, lxxvi. 471, 1901), and M. O. Wyss (*Beitr. z. klin. Chir.*, xxvi. 631, 1900). E. Kirmisson (*Traité des maladies chirurgicales*, 412, 1898) has related a case of anal atresia operated on with apparent success soon after birth; the infant, however, died, and it was then found that there existed a valvular obstruction of the duodenum in addition to the anal defect.

Congenital intestinal obstruction may be situated in the jejunum. This seems to have been the case in J. Thomson's interesting specimen (*Trans. Edinb. Obstet. Soc.*, xvii. 128, 1892) in which a small bit of gut, blind at both ends, intervened between the distended duodenum and the rest of the small intestine; it was fixed in the shape of a horseshoe by a little tongue-like flap of mesentery; the child, from whom the preparation was obtained, died when ten days old. Other instances of jejunal obstruction were reported by Pied (*Journ. de méd., chir., pharm.*, iii. 227, 1802), Kirchner (*Berl. klin. Wchnschr.*, xxiii. 444, 1886), and F. C. Turner (*Trans. Path. Soc. Lond.*, xxxviii. 145, 1886–87). The fæces which pass from the anus in these cases are usually colourless or earthy in appearance, a fact which H. Salus

(*Prag. med. Wchnschr.*, xxi. 529, 1896) made use of to diagnose an intestinal anomaly in the case of a fœtus which was being born by the breech. The absence of the dark green meconium, however, is not a constant phenomenon, for in J. Thomson's patient (*loc. cit., supra*) some was passed several days after birth; it is very difficult to explain this circumstance.

The ileum is apparently a common seat of intestinal obliteration, a fact which may find its explanation in the frequent presence of a Meckelian diverticulum here and in the traction produced by it (J. B. Sutton, *Amer. Journ. Med. Sc.*, n.s., xcviii. 457, 1889). Probably most of the cases reported as instances of congenital occlusion of the small intestine affect the ileum; many references to these are to be found in the *Index Catalogue* (vol. vii. pp. 19, 61, 1886; n.s., vol. viii. pp. 207, 277, 1903). The seat of obstruction is frequently the place where the small intestine becomes continuous with the large. Multiple constrictions have also been noted (C. Thorel, *München. med. Wchnschr.*, xlvi. 1202, 1899; F. Gaertner, *Jahrb. f. Kinderh.*, n.F., xx. 403, 1883; etc.).

Obliteration of the large intestine above the sigmoid flexure is not common; below that level it is much less rare, and generally takes the form of atresia ani or of imperforate rectum, anomalies which are dealt with along with the malformations of the pelvic organs (p. 563). In some cases of atresia of the small intestine, the colon may be filiform or absent altogether; but even when the upper part of the bowel is normal, the lower part may be absent (Charon et Vervaeck, *Ann. Soc. belge de chir.*, viii. 71, 1900), or greatly contracted (E. Kirmisson, *Traité des maladies chirurgicales*, 415, 1898).

Various opinions have been expressed regarding the mode of production of intestinal atresia in the fœtus. At first sight it seems probable that the cause may be fœtal peritonitis, and that, in this anomaly at least, the pathological or nosological theory of teratogenesis holds good; but there are difficulties in the way, for, in order to explain some of the reported cases, it must be supposed that the peritonitis is developed at a very early date in antenatal life, at a time in fact when it is not easy to understand how an inflammation can exist. G. Durante and L. Siron (*Bull. et mém. Soc. obst. et gynéc. de Paris*, p. 51, 1897) incline towards the view of arrested development, and think that failure of the artery which ought to supply the affected part of the intestine is the cause of the absence or contracted state of that part.

Miscellaneous Gastric and Intestinal Anomalies.

In addition to anomalies in the position of the stomach such as occur in connection with diaphragmatic hernia and transposition of the viscera, that organ may show *hour-glass constriction* or contraction of an antenatal kind (J. H. Musser, *Phila. Med. Times*, xiv. 331, 1883–84). It has been supposed that this may indicate an atavistic tendency or return to the condition of the stomach met with in some of the lower animals; but it may be accounted for in the same way as is intestinal constriction. Dwight (*Amer. Journ. Med. Sc.*, n.s., cxxvi. 581, 1903) has recently met with a well-marked case; R. Sievers saw another instance in 1899 (*Berl. klin. Wchnschr.*, xxxvi. 325, 1899). Various *anomalies in the position of the intestines* have been recorded. Guyot (*Bull. Soc. d'anat. et physiol. de Bordeaux*, xix. 82, 1898), for instance, found the cæcum in the right hypochondrium attached to the lower surface of the liver by a peritoneal fold; the ascending colon was absent. I also have found the cæcum displaced; it was nearly mesial in one case, and in another was higher up than normal. In fact this part of the intestine and the appendix vermiformis attached to it would seem to be frequently displaced (R. B. Young, *Journ. Anat. and Physiol.*, xix. 98, 1885; J. L. Faure, *Bull. Soc. anat. de Paris*, lxx. 9, 1895; Gentés, *Bull. Soc. d'anat. et physiol. de Bordeaux*, xx. 365, 1900; H. A. Sifton, *Clin. Rev.*, Chicago, xvi. 106, 1902; etc.). All these malpositions doubtless represent stages in the evolution of the intestine which are normally transitory, but may be rendered permanent by some cause (fœtal peritonitis (?), arrested development).

Since the *appendix vermiformis* has come to be studied and operated upon, its anomalies have also become better known. It may be entirely absent (*e.g.* in G. Piquand's case, *Bull. et mém. Soc. anat. de Paris*, lxxv. 602, 1900, and in J. M. Swan's case, *Univ. Med. Mag.*, viii. 194, 1895–96); or it may be unusually large (E. Fawcett, *Journ. Anat. and Physiol.*, xxix. 498, 1894–95); or it may open into the small intestine (Thoyer, *Bull. Soc. anat. de Paris*, lxviii. 205, 1893). In Altuchoff's case (*Anat. Anz.*, xxii. 206, 1902) the appendix passed upwards for a distance of 15 cm. behind the cæcum; then it turned to the left and downwards for a distance of 10 cm., lying in the mesentery of the small intestine; and finally it ended in a bundle of fibrous tissue 4 cm. long.

Into the subject of *congenital inguinal and femoral hernia* I do not consider it my duty to enter in this work. These anomalies are fully described in every system of surgery, and their bibliography may be found in the *Index Catalogue* (vol. vi. 152, 1885; 2 s., vol. vii. 13, 1902). The same remark applies to congenital hydrocele (*Index Catalogue*, vol. vi. 548, 1885; 2 s., vii. 506, 1902); but I may mention that I have met with a case of congenital inguinal hernia in an infant whose father suffered from congenital hydrocele. The mode of production of both these anomalies in antenatal life needs no elucidation. For a good description of them both the reader is referred to E. Kirmisson's *Traité des maladies chirurgicales d'origine congénitale*, pp. 342–375, 1898.

Anomalies of Liver and Gall Bladder.

Malformations of the liver have been already alluded to under the headings of hernia of the diaphragm and of the umbilical cord; but this organ may show anomalies apart from these states. Accessory livers (*hepata succenturiata*) have been described by W. Gruber (*Arch. f. path. Anat.*, lxxxii. 476, 1880), Simpson (*Month. Journ. Med.*, Lond., xx. 179, 1855), and Van Buren (*New York Med. Times*, iii. 126, 1853–54); and accessory lobes or an anomalous arrangement of lobes are not very uncommon (E. Laget, *Bull. Soc. anat. de Paris*, xlix. 42, 1874; Micheleau, *Journ. de méd. de Bordeaux*, xxvi. 228, 1896; and N. Moore, *Trans. Path. Soc. Lond.*, xxxiii. 192, 1881–82; Planteau, *Journ. de méd. de Bordeaux*, xiv. 347, 1884–85). In complete transposition of the viscera, the liver, like the other abdominal organs, exhibits the characteristic inversion; and the parts on the under surface of it may show this inversion as a separate anomaly. The Spigelian and quadrate lobes may be absent (A. R. Simpson, *Edinb. Med. and Surg. Journ.*, vi. 1045, 1860–61). Cystic disease of the liver has been met with in the fœtus (J. C. B. Smallman, *Lancet*, ii. for 1859, 573; Bagot, *Dublin Journ. Med. Sc.*, xciii. 265, 1892); and cases of malignant disease, both carcinomatous (E. Noeggerath, *Deutsche Klinik*, vi. 496, 1854) and sarcomatous (R. W. Parker, *Trans. Path. Soc. Lond.*, xxxi. 290, 1879–80), have been reported.

Absence of the gall bladder has been observed in a fairly large number of cases. Recent instances have been noted by A. A. Eshner (*Med. News*, lxiv. 548, 1894), by K. Thue (*Festskr. . . . Prof. Heibergs*, Kristiania, p. 137, 1895), by O. Giese (*Diss. inaug.*, Leipzig, 1896), and by A. Latham (*Proc. Anat. Soc. Gr. Brit. and Ireland*, p. xxxix., 1898); references to the older cases of W. N. Baker, G. H. Bergmann, H. J. Cholmely, Cuynat, Gaultier de Claubry, Godélier, F. Godfrey, J. J. Huber, J. Lynch, Rambault and Schachmann, M. Roth, H. B. Sands, A. R. Simpson, G. Targioni, Tozzetti, E. Thomas, D. M. Trimble, J. H. Vergue and L. O. J. Leignel, Wiedemann, and P. Wolfartus are given in the *Index Catalogue* (vol. v. p. 249, 1884). Eshner's case was that of a rachitic child who died of broncho-pneumonia at the age of two years; he never had jaundice and yet there was absence of the gall bladder; the liver was otherwise normal, and there was a supernumerary spleen. In R. Müller's specimen (*Diss. inaug.*, Kiel, 1893), however, the defect of the gall bladder was combined with atresia of the duodenum, atresia of the left ureter, a cystic condition of the kidneys, and anomalies of the outer and middle ear and palate; and in Gevaert's (*Arch. de tocol.*, xxi. 588, 1894) there was atresia ani and absence of the right thumb as well as no gall bladder. Complete absence of the gall bladder is the normal condition in some animals, and so this arrested development in man has been regarded as atavistic; but it may arise apparently from early obliteration in conjunction with obliteration of the bile ducts. Of this latter state J. Thomson has reported an interesting case (*Trans. Edinb. Obstet. Soc.*, xvii. 191, 1892), in which the gall bladder was very small, its posterior end and part of the cystic duct being entirely obliterated; the infant, a fifteenth child, only survived birth a few hours, and showed other structural defects (hare-lip, cleft palate, and anomalies of outer ears, of both hands, and of the heart). J. Thomson has also given a very good account of *congenital obliteration of the bile ducts* (*Trans. Edinb. Obstet. Soc.*, xvii. 17, 1891–92), with literature list and tabular analysis of cases. I have referred to the subject in Vol. I. of this Manual (p. 363), for the anomaly has been ascribed to fœtal disease (*e.g.* peritonitis); but as it has also been thought to be due to an arrested development (a view favoured by Thomson, *loc. cit.*, p. 45) it requires to be mentioned here. It is one of the morbid states lying on the border-line between fœtal pathology and embryonic pathology.

Other anomalies of the liver, gall bladder, and associated ducts have been reported. Griffon (*Bull. Soc. anat. de Paris*, lxix. 777, 1894), for instance, found the bladder situated in a depression on the antero-superior surface of the liver; there was a small accessory right lobe. A. R. Simpson (*Trans. Edinb. Obstet. Soc.*, xx. 13, 1895) noted extensive fusion of the right and left halves of a fœtal liver below the ductus venosus. E. Cruveilhier (*Bull. Soc. anat. de Paris*, xxxv. 66, 1860) saw a double gall bladder, with a single neck, giving origin to two cystic ducts. Brun (*Bull. et mém. Soc. de chir. de Paris*, n.s., xxiii. 207, 1897) has reported dilatation of the bile ducts, probably antenatal in origin.

Miscellaneous Malformations of Abdominal Viscera.

The spleen may sometimes be *absent*, as in C. Taruffi's specimen (*Mem. d. r. Accad. d. sc. d. Ist. di Bologna*, 5 s., iv. 73, 1894), in which there was also absence of the pancreas, suprarenal capsules, genitals, prostate, colon, and rectum. Other instances have been reported by F. D. Hirschfeld (*Arch. d. Heilk.*, xii. 190, 1871), Jelenski (*Berl. klin. Wchnschr.*, xvii. 704, 1880), G. Martin (*Bull. Soc. anat. de Paris*, 2 ed., i. 40, 1841), and H. L. F. Robert (*Arch. f. Anat. Physiol. u. wissensch. Med.*, p. 57, 1842). *Supernumerary or accessory spleens* ("splenunculi" or "lienculi") are not very rare; I figured one (in an otherwise normal infant) some years ago (*Introduction to the Diseases of Infancy*, Pl. vi., Fig. 2, p. 79, 1891); P. Claisee (*Bull. Soc. anat. de Paris*, lxix. 829, 1894) has reported an instance of two spleens and numerous supernumerary spleens in a child (nine years old) suffering from congenital heart disease; and other cases have been noted by L. Calori (*Sulla duplicità congenità della milza*, Bologna, 1863), W. H. Bainbrigge (*London Med. Gaz.*, xxxviii. 1052, 1846), W. Cheselden (*Philos. Trans.* (1700–1720), 2 ed., iv.–v. 252, 1831), J. J. Harderus (*Miscel. Acad. nat. curios.*, Dec. 3, ix.–x. 127, 1706), Jolly (*Bull. Soc. anat. de Paris*, 5 s., ix. 745, 1895), and L. Rocher (*Journ. de méd. de Bordeaux*, xxxiii. 833, 1903). *Transposition of the spleen* is seen in general inversion of the viscera.

Anomalies of the *suprarenal bodies* have been noted. Their *absence* or rudimentary state in cases of anencephaly has been already referred to (p. 346); but they may be defective in other types of monstrosity, as in Taruffi's case of agenosoma (*Mem. d. r. Accad. d. sc. d. Ist. di Bologna*, 5 s., iv. 73, 1894), and they may be congenitally absent where no malformations exist but where the skin is bronzed (J. K. Spender, *Brit. Med. Journ.*, p. 768, 1858). In cases of Addison's disease where one of the suprarenals is absent (J. W. Legg, *St. Barth. Hosp. Rep.*, x. 225, 1874), it does not, of course, follow that the defect was congenital. H. D. Rolleston (*Brit. Med. Journ.*, i. for 1895, p. 629) has referred to various anomalies of the adrenals, including the presence of *accessory* ones. These accessory suprarenal bodies have considerable pathological importance: they may be found in the neighbourhood of the normal organs and under the capsule of the kidney (G. N. Pitt, *Trans. Path. Soc. Lond.*, xlv. 141, 1894), or in the semilunar ganglion (Jaboulay, *Lyon méd.*, lxv. 300, 1890), or in the broad ligament (Marchand, *Arch. f. path. Anat.*, xcii. 11, 1883), or in connection with the vas deferens (F. Friedland, *Prag. med. Wchnschr.*, xx. 145, 1895), or (most frequently) in the kidney. In these positions the accessory suprarenals may take on malignant characters and produce tumours, carcinomatous, adenomatous, or lipomatous in their nature. Renal tumours developed from these adrenal "rests" or accessory glands are called *hypernephromata*; they vary from a cherry to a child's head in size; and form very interesting evidence in support of the teratological theory of the origin of tumours. A very considerable literature has grown up round hypernephromata, and among many references (the list of which may be found in the *Index Catalogue*, 2 s., viii. 714, 1903) I may specially single out those of Cullen (*Johns Hopkins Hosp. Bull.*, vi. 37, 1895), F. Harbitz (*Norsk Mag. f. Lægevidensk.*, 4 R., xiv. 521, 1899), A. O. J. Kelly (*Phila. Med. Journ.*, July 30, 1898), O. Lubarsch (*Arch. f. path. Anat.*, cxxxv. 149, 1894), E. J. M'Weeney (*Brit. Med. Journ.*, i. for 1896, p. 323), B. H. Buxton (*Journ. Path. and Bacteriol.*, vii. 221, 1900–01), A. Jenckel (*Deutsche Ztschr. f. Chir.*, lx. 500, 1901), T. N. Kelynack (*Chir. Journ.*, xx. 335, 1902), and A. Pepere (*Monitore zool. ital.*, xiv. 261, 1903).

Anomalies of the *pancreas* are comparatively rare. Accessory or succenturiate pancreas (*Nebenpankreas* of the Germans) has been described by E. Montgomery (*Trans. Path. Soc. Lond.*, xii. 130, 1860–61), C. Apollonis (*Gazz. d. osp.*, viii. 196, 1887), and Reitmann (*Anat. Anz.*, xxiii. 155, 1903). In a case reported by J. Symington (*Journ. Anat. and Physiol.*, xix. 292, 1885) two processes of pancreas passed round the upper part of the descending portion of the duodenum, and, with the aid of the head of the gland, formed a complete ring round the intestine. In some other instances the pancreas has established relations with the gastric and intestinal walls (C. Gegenbauer, *Arch. f. Anat. Physiol. u. wissensch. Med.*, 163, 1863; E. Wagner, *Arch. d. Heilk.*, iii. 283, 1862; A. Weichselbaum, *Ber. d. k. k. Krankenanst. Rudolph-Stiftung in Wien*, 379, 1884; F. A. Zenker, *Arch. f. path. Anat.*, xxi. 369, 1861). G. Sangalli (*Gazz. med. lomb.*, lvi. 31, 1897) has met with a double pancreas, one part lying in front of the other, and with an accessory lobe arising from the upper border of the gland. Anomalies of the *pancreatic duct* also exist: in a case reported by Bodinier (*Bull. Soc. anat. de Paris*, xviii. 262, 1843) the duct opened into the duodenum 4 cm. above the bile duct; and other malformations were described by M. Sée (*Compt. rend. Soc. de biol.*, 2 s., iv. 1, 1858).

Malformations of the kidneys and bladder fall to be described in the next chapter, for although neither of these organs is pelvic in position in the fœtus it is convenient to discuss their anomalies with those of the pelvis. I may note here that *vascular anomalies* in the abdomen are met with, but have been little investigated. M. Cavasse (*Bull. Soc. anat. de Paris,* 811, 1897) has met with a case in which the vena cava inferior terminated below the renal veins in a cone, and had no communication with the right femoral vein except through an enlarged spermatic vein; there had been an arrested development of the right posterior cardinal vein. Lauber (*Anat. Anz.*, xix. 590, 1901) has seen a specimen in which the two cardinal veins persisted to the level of the kidneys, where there was a cross union; the inferior vena cava came from the right renal vein; and the larger trunk passed upwards, taking the course of the vena azygos major. Other anomalies of the vena cava inferior have been reported by J. Kollmann (*Anat. Anz.*, viii. 75, 97, 1892–93), by Lagneau (*Bull. Soc. anat. de Paris,* xxviii. 344, 1853), and by H. J. Waring (*Journ. Anat. and Physiol.*, xxviii. 46, 1893–94).

Congenital Umbilical Tumours.

A few words are not out of place regarding antenatal growths originating in the umbilicus. The so-called granulomata which form immediately after the fall of the cord do not belong to this group, although some writers would admit them. No case of umbilical cancer in a new-born infant has been reported; but cases of nævus maternus of the umbilical region may in later years become malignant; it is also believed that cancer may develop in a persistent Meckelian diverticulum attached to the navel. Dermoid cysts may be found at the umbilicus; so may cysts developed from Meckel's diverticulum and having a structure closely resembling that of the wall of the intestine. These latter growths have been called vitelline or diverticular cysts, and are closely related to the umbilical adenomata or vitelline tumours (called in a loose fashion entero-teratomata). E. Kirmisson (*Maladies chirurgicales d'origine congénitale,* p. 214, 1898) gives a good description of them, while L. Pernice (*Die Nabelgeschwülste,* Halle a. S., 1892) has a valuable monograph (with bibliography) dealing with them and with all other forms of umbilical neoplasm. Parasitic fœtuses attached to the umbilicus or lying in the abdominal cavity belong to the polysomatous and not to the monosomatous terata.

CHAPTER XXVIII

Merosomatous Terata (*cont.*): Malformations of the Pelvic Organs: Extroversion of the Bladder; Definition, Synonyms, Historical Notes, Clinical Features, Morbid Anatomy (in the Male and in the Female), Cloacal Variety, Teratogenesis, Literature; Urinary Umbilical Fistulæ; Miscellaneous Malformations of the Bladder (Double Bladder, Diverticula); Malformations of the Kidneys (Absence, Single Kidney, Displacement, Lobulation, Accessory Kidney, Cystic Kidney); Malformations of the Ureters; Malformations of the Penis (Absence, Duplication or Diphallus, Double Urethra, Penile Canals, Atresia of Urethra, Epispadias, Hypospadias); Malformations of the Testicles; Malformations of the Female Genitals; Malformations of the Anus and Rectum; Hermaphroditism.

THE regional method of dealing with the subject of Teratology is less satisfactory in its relation to the malformations of the pelvis and its viscera than to those of any other part of the body. The bladder and some of the genital organs are abdominal in position in fœtal life although they are pelvic in the adult, and the question therefore arises whether their anomalies are to be described among the abdominal or among the pelvic terata. In the scheme of classification on p. 235 I got over the difficulty by grouping the pelvic and abdominal anomalies together; but for the purposes of chapter-division it is necessary to separate them, and, for convenience, I place the malformations of the bladder and the associated organs (the kidneys and ureters) and of the genitals with the pelvic malformations (*lecano-terata*). With this word of explanation I proceed with their description, taking as the type-malformation extroversion or ectopia vesicæ.

Extroversion of the Bladder.

When the anterior abdominal wall in the hypogastric region and the anterior bladder wall are both defective, the anomaly known as extroversion of the bladder is produced. It has also been called *exstrophy of the bladder*, but the proper spelling according to the analogy of the Greek derivatives would be ecstrophy (Murray's *New Engl. Dict.*, iii. E. p. 453). Other synonyms are ectopia vesicæ, inversion of the bladder, prolapse of the inverted bladder, and ectropion vesicæ; but *inversion of the bladder* has come to be applied to the acquired condition in which (in females) the bladder is prolapsed through the urethra, and the other names have no advantages over extroversion. C. Taruffi (*Storia della teratologia,* vii. 406, 433, 1894), in order to emphasise the fact that there is fissure of the abdominal wall in the hypogastric region and separation of the pubes (*τό ἦτρον*), has suggested *hypogastro-etro-schisis*, a perfectly unmanageable vocable, which, after all, does not draw the attention to the defect in the bladder. The German expression, *Bauchblasenschambeinspalte*, cannot be rendered by any suitable English equivalent. For these reasons I retain the term "extroversion of the bladder."

The *historical records* of vesical extroversion go far back. Perhaps the first known case is that found on the Chaldean tablets (*Teratologia*, i. 132, 1894), in which a child is described as wanting the penis and the umbilicus. At any rate, an authentic instance of congenital aperture of the abdomen and bladder was reported by Ambrosinus (editor of Aldrovandus' *Historia Monstrorum*, p. 507, 1641). Several cases were made public in the seventeenth century, including that of Cornelius Stalpart vander Wiel (*Zeldzame Aanmerkingen*, p. 307, 1686) under the title of *Een Kint sonder Navel geboren*, and that of C. L. Gockelius (*Miscel. Acad. nat. curios.*, Dec. ii. Ann. v., obs. 43, p. 84, 1687), graphically described as "vesica spongiosa extra abdomen posita cum defectu penis." In the eighteenth century the nature of the malformation came to be better understood, for it was recognised in 1767 by Devilleneuve (cited by Taruffi, *op. cit.*, vii. 432) that the tumour, seen projecting from the abdomen above the symphysis pubis, was not a simple hernia of the bladder but was the posterior vesical wall itself, the bladder as well as the abdominal walls being defective anteriorly. James Mowat, writing in 1735 (*Med. Essays and Observ. Edinb.*, iii. 276), was evidently quite at a loss to explain the appearances in a typical case of extroversion of the bladder, and was careful to entitle his article "An Account of a Child born with the Urinary and Genital Organs preternaturally formed." In the nineteenth century many details of the morbid anatomy of ectopia vesicæ were carefully investigated, and considerable progress was made with the elucidation of its teratogenesis. A great literature has grown up round the subject; how great, the reader has only to consult the *Index Catalogue* of Washington to realise (vol. ii. 81, 1881; vol. ix. 408, 1888; vol. xv. 128, 1894; 2 s. vol. ii. 371, 1097, etc.).

The *clinical history* of cases of extroversion of the bladder begins as a rule with birth. There is, in most cases, nothing during the pregnancy to cause the mother or her medical attendant to suspect any anomaly in the infant. After the birth of the child, however, the mother may recall a maternal impression, a circumstance which, as we have seen, is by no means peculiar to this special type of monstrosity. In a case, the details of which were communicated to me by Dr. W. Iverach Robertson in 1891, the maternal impression was the hearing of the birth of an infant about whose sex there was some doubt (absence of penis), and the woman gave birth to a child with ectopia vesicæ and epispadias seven months later. In Mowat's case (*loc. cit.*) the mother, when about two or three months pregnant, was struck in the abdomen with a cow's horn, but was apparently more frightened than hurt.

Postnatal life is not gravely interfered with in extroversion of the bladder, save in the cases in which the intestine opens into the malformed bladder. In the uncomplicated cases adult life has often been reached, although the individual suffers great inconvenience from the constant dribbling of urine and from catarrhal inflammation of the bladder. Possibly on account of the continuance of postnatal life, possibly also because the anomaly is not very rare, many cases have been reported, as the extensive bibliographies in the *Index Catalogue* abundantly testify. As it so happens I have only had an opportunity of examining cases in which gastroschisis of an advanced degree was also present, and in which, therefore, the ectopia vesicæ was not the most obvious feature. I reproduce, however, as a typical instance of the deformity, a photograph which I received from Dr. Michin of Charkow in 1897 (Fig. 78). The child was born spontaneously after a thirteen hours labour; it was a female and showed pelvis fissa and prolapsus uteri incompleta, as well as ectopia vesicæ; on the twelfth day after birth she died from hæmorrhage from the bladder (*Trans. Edinb. Obstet. Soc.*, xxii. 108, 1897). The frequency of extroversion of the bladder has been placed at 1 in

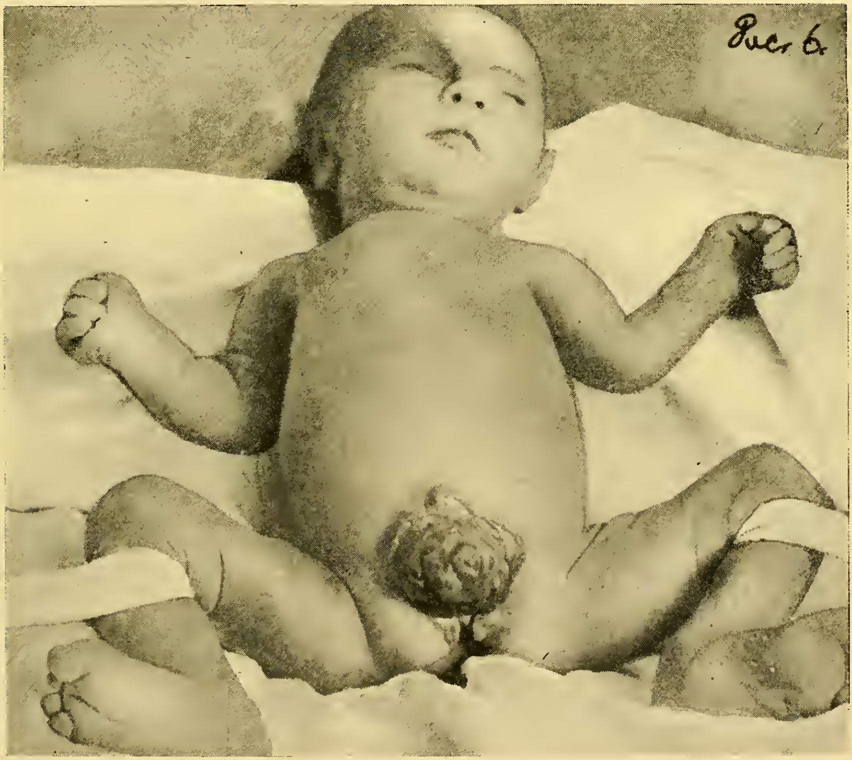


Fig. 78.—Dr. Michin's Case of Ectopia Vesicæ in a Female Infant.

50,000 births; it is much commoner in males than in females, in the proportion of six or seven to one.

The distressing circumstances of a patient with vesical ectopia (constant dribbling of urine, ulceration and excoriation of neighbouring parts, risk of ascending pyelo-nephritis, urinous and ammoniacal odour, associated genital malformations) have been the cause of the many attempts, several of them most ingenious, that have been made to correct the deformity by surgical interference. In the first place, there have been the methods in which flaps of skin from adjacent parts have been used to close in the abdomen (plans of Roux, Thiersch, Wood, Le Fort, and others); then there have been the various devices by which it has been endeavoured to turn the stream of urine into the lower part of the intestine (Simon, Smith, Lloyd, Holmes, Tuffier), or into the urethra itself (Sonnenburg, Zesas, Segond); and in the third place, there have been attempts to close the bladder itself by direct sutures and to approximate the two halves of the symphysis pubis (Gerdy, Rigaud, Wyman, Trendelenburg, Pousson). The difficulties in the way of complete success by any of these methods are formidable. To use flaps of adjacent skin produces a urinary reservoir which is not lined by vesical mucous membrane, and in which concretions are almost certain to form. To turn the ureters into the rectum or sigmoid flexure has given good results in some cases, although the lower bowel is not fitted physiologically to act as a bladder or cloaca. Direct suture of the vesical walls is the most scientific and the most hopeful procedure, if the difficulty of the reproduction of the sphincter can be got over. There is still work for the courageous and resourceful surgeon in this department of reparative intervention; and there is pressing need, for the only alternative to operation is the wearing of a urinal. Some doubtful cases of antenatal cure or partial cure of this malformation have been recorded (E. Küster, *Verhandl. d. Berl. med. Gesellsch.*, viii. pt. i. 4, 1877); and spontaneous cure may apparently take place also after birth (L. Lichtheim, *Arch. f. klin. Chir.*, xv. 471, 1873). Before leaving the clinical aspects of extroversion of the bladder I may add that some instances of pregnancy and labour have been recorded (C. Taruffi, *op. cit.*, vii. 462, 1894), in two or three of which the birth of the child was rendered long and difficult.

The *morbid anatomy* of extroversion of the bladder differs considerably according as the patient is a male or a female; and I shall, therefore, follow Taruffi's plan (*op. cit.*, vii. 435) and describe it first in the male subject and second in the female. Thereafter I shall consider the associated malformations and shall pay special attention to those cases in which the intestine opens into the bladder (*cloacal extroversion*).

In the *male subject* the most striking feature is the projection of a red vascular mass, somewhat rounded in size and elastic in consistence, in the hypogastric region, just above the penis (malformed or normal). In the lower part of the mass are two openings (lower ends of ureters) from which urine dribbles away and keeps the whole surface moist; the openings are situated, one on each side of the middle line, at an equal distance from it. The surface of the mass is really the mucous membrane of the posterior wall of the bladder, and by pushing it inwards with the finger a bladder cavity can be to some extent produced; here and there the vesical mucosa may take on cutaneous characters, and elsewhere it may show granulations and bleed on handling. The ureteric openings may lie in depressions between the folds of the mucosa or may form little projections or even tubular prolongations. Sometimes the ureters lie close together and have a single opening; sometimes one ureter (with its corresponding kidney) is absent, the other opening by itself at one side; at other times both the kidneys and their ureters are absent; and at others, they open into the rectum, a circumstance which suggested one of the methods of surgical interference to which I have referred. Behind the bladder the ureters may show cyst-like dilatations.

The umbilical cord, in the form of a cord, may be absent, and then the umbilical vessels may enter the abdomen separately or may run to it in the membranes; when this is the case no proper umbilical scar is visible as the infant grows older. In other instances the vessels (consisting sometimes of only one artery and a vein) are collected together in a distinct funis which enters the abdomen above the level of the vesical extroversion; then the fall of the cord is followed by the formation of a cicatrix either in the normal position or a little lower down. Sometimes the cord is attached to the apex of an umbilical hernia (P. Bockenheimer, *Arch. f. klin. Chir.*, lxix. 669, 1903).

There is nearly always want of union of the pubic bones at the symphysis; indeed there is usually a wide separation of them, bridged over by a fibro-muscular structure, the so-called infrapubic ligament. This separation of the pubic bones is normal in some animals, and it may occur in the human subject quite apart from extroversion of the bladder (Schauta, *Centrlbl. f. Gynäk.*, xxiii. 1047, 1899). There may be other deformities of the pelvis as well as pubic diastasis: the pelvic cavity, for instance, may be diminished in size by the upward displacement of the sacrum and coccyx or by forward inclination of the promontory of the sacrum due to what may be called sacral lordosis or (less correctly) pelvic inversion.

A very commonly associated malformation is epispadias, the penis being divided superiorly and the urethral canal laid open. The corpora cavernosa are often defective, so that the penis appears as if it consisted of little more than the glans with its prepuce. The scrotum may have a single or a double cavity and may contain both testicles; but it is not uncommon for the latter organs to be intra-abdominal in position or to be situated at some point in the inguinal canals. The vasa deferentia may open directly into the urethra. The genital organs may be still more rudimentary, the penis and scrotum being either entirely absent or represented by tags of skin. There may be two genital tubercles situated at some distance from each other, as in the specimen of gastroschisis kindly given me by Professor Stephenson of Aberdeen (Fig. 79).

In the instances of extroversion of the bladder that survive birth the anus is usually normal; but atresia ani has been several times noted in those that die in the early days of life. In some cases the intestine opens into the bladder, and about these something will be said immediately. In yet other cases there is hernia of the umbilical cord or in the inguinal and scrotal regions; even perineal hernia has been noted in association with extroversion of the bladder (G. Krüger, *Diss. inaug.*, Rostock, 1872).

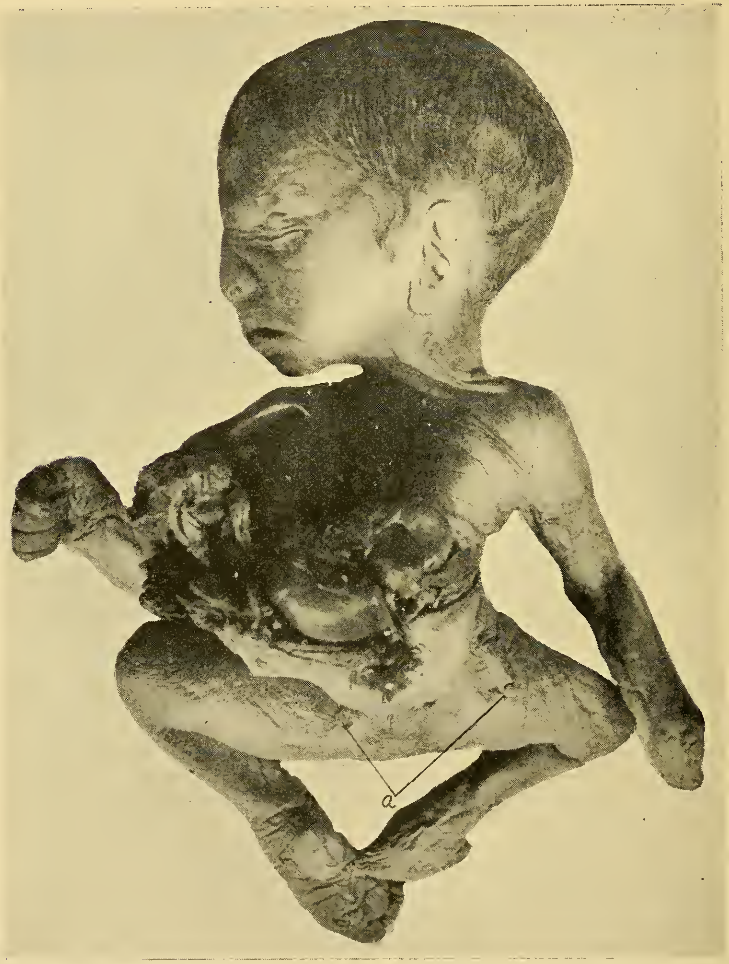


Fig. 79.—Case of Gastroschisis and Double Genital Tubercle (*a*). Specimen No. 200.

In the *female* subject, extroversion of the bladder is, as has been said, much rarer than in the male. Possibly this difference is due to some peculiarity in the embryology of the hypogastric region in the female as compared with the male. A similar reason may perhaps explain why it is that vesical extroversion in the female is often of an incomplete kind. Well-marked cases present the same features as in the male: there is the red projection in the hypogastric region with the two ureteric openings, there is separation of the pubic bones, and usually the anterior urethral wall is absent leaving the posterior wall exposed (epispadias). Some features, however, are peculiar to the female. The vagina has a transverse opening, is somewhat short, and may show a degree of prolapse. The uterus may be bicornate. The perineum usually is short and so the anus is situated further forward than is normal. The rectum may open into the vagina (vulvar anus). The clitoris may be absent or may be represented by two widely separated tubercles lying one at the anterior end of each labium minus. The labia majora do not usually unite in a recognisable mons veneris, and may only be represented by skin tags.

In the male, extroversion of the bladder and epispadias although often associated can be easily separated from each other; but in the female these two malformations are often very difficult of differentiation, for the urethra is short and its malformations are apt to be insignificant. Further, there would appear to be intermediate cases having some of the characters of vesical ectopia and some of epispadias. Such an intermediate type I recorded under the name of epispadias in 1896 (*Edinb. Hosp. Rep.*, iv. 249, 1896); but it might with some show of reason have been called extroversion of the bladder of a very slight degree, or "subsymphysial vesical exstrophy." In these cases the symphysis pubis is usually closed, and in this character they resemble epispadias; on the other hand, a small part of the anterior bladder wall in the symphysial region is absent (allowing prolapse through it of the mucous membrane), and in this character they approximate to vesical extroversion. In my article above referred to, I have discussed at some length both female epispadias and subsymphysial exstrophy, and have given a bibliography of cases; to it the reader who is interested in this obscure corner of teratology may have recourse.

Finally, a few sentences may be devoted to the description of the morbid anatomy of the cases of extroversion of the bladder which have been called *cloacal*. These are the instances in which the intestine ends in the open bladder; and Taruffi (*op. cit.*, vii. 464, 1894) has gathered together from literature forty-one of them, to which may be added P. Bockenheimer's specimen (*Arch. f. klin. Chir.*, lxix. 669, 1903). In this last-named case the patient was a male infant, three days old. In the middle line of the abdomen between the openings of the ureters there was a proboscis-like projection which consisted of the cæcum and ileum, prolapsed and split; below this was another opening which was found, on post-mortem examination, to be the end of a short large intestine which ended blindly in the pelvis. This may be regarded as a typical case of the cloacal form of extroversion in the male. From the intestinal openings meconium can be seen protruding at and soon after birth, and the prolapsed bit of bowel may simulate a penis. There is generally atresia ani in these cases. In the female subject the uterus is usually double, and there may also be duplicity of the vagina; in such circumstances the vaginæ may open within the area of extroversion in the near neighbourhood of the ureters. Unusual cloacal combinations have been noted, as when one vagina opens on the surface and the other ends blindly, or when one vagina opens into a ureter, or when both vaginæ end blindly. In the male, the vasa deferentia have been found opening into the extroverted bladder; and in a very remarkable case (P. Gast, *Diss. inaug.*, Greifswald, 1884) the vagina on the left side and a testicle on the right side were connected with the open bladder. Sometimes a peritoneal fold (recto-vesical ligament) has been found passing from the posterior wall of an extroverted bladder between the two halves of the double uterus to be inserted on the rectal walls. In these complicated cloacal forms it is common to find malformations of the intestine within the abdomen, such as absence of the appendix vermiformis, displacement of the small intestine, etc.

As will have been gathered from the preceding description of vesical extroversion, *associated malformations* are not uncommon. Among these may be mentioned spina bifida, especially of the sacral region (O. Grundies, *Diss. inaug.*, Berlin, 1883), spinal scoliosis, umbilical hernia, club-foot (Hamaide, *Bull. Soc. de méd. prat. de Paris*, p. 310, 1891), hare-lip, non-descent of the testicles (A. Broca, *Bull. Soc. anat. de Paris*, lxii. 791, 1887).

The *teratogenesis* of extroversion of the bladder is a subject of great complexity. The older writers looked, as usual, for a mechanical or pathological (nosological) cause. Some found it in overdistension of the fœtal bladder with urine; the result was bursting of the urethra (epispadias), of the bladder (extroversion), and of the tissues of the symphysis pubis (pubic diastasis); the cause of the overdistension of the bladder was found in blocking of the urethra or in a dropsical tendency. Others looked for a determining cause in external violence or injury suffered by the pregnant woman or in mental impressions. Shortness of the cord or of the vessels entering into it was another alleged cause of extroversion of the bladder, and brevity of the vitelline duct was added to it to explain the associated intestinal malformations. Traction by the vitelline duct has been a favoured theory, Ahlfeld especially pressing it strongly (*Die Missbildungen des Menschen*, ii. 206, 1882). The duct, as is well known, arises from the intestine in the region of the ileum; and it was thought, therefore, that in this fact lay the explanation of the cloacal forms in which it was the ileum that opened into the extroversion. At the same time it must be admitted that this theory does not explain all the facts, and it was found necessary to bring forward blocking of the urethra and overdistension of the allantois to account for the rupture of the anterior bladder wall. At the present day the theory of mechanical origin may be said to be merged in that of disordered embryology (to which I shall refer immediately).

The idea of disease as a cause of extroversion of the bladder was once popular, and erosions and ulceration of the anterior abdominal and vesical walls were regarded as sufficient causes; but with an increase in our knowledge of the principles of antenatal pathology the nosological theory has ceased to have a prominent place in teratogenesis. It is no longer necessary to have recourse to such morbid causes to explain the open state of the abdomen and bladder, for arrested ontogenesis is sufficient; fœtal peritonitis need not be invoked to account for the opening of the bowel into the urinary bladder, since the persistence of the entodermal cloaca is a sufficient explanation.

The only reason why the embryological theory of the production of extroversion of the bladder has been incomplete lies in our imperfect knowledge of all the details of the ontogenesis of the bladder and surrounding parts. The early writers of the nineteenth century, including Meckel, although they believed in arrested development as the great teratogenic cause, were hampered in their efforts to explain all the features of the vesical malformation by defective information, or by erroneous preconceptions regarding the development of the bladder. A great difficulty seemed to exist in the fact that the bladder cavity was open, for it was not known that there was any stage in ontogenesis when this organ was in this state, and there was no evidence that it was derived from two symmetrical halves, for it was believed to be derived from the allantois, which is a single and not a double organ. F. Tourneux (*Journ. de l'anat. et physiol.*, xxiv. 503, 1888; xxv. 229, 1889) and Durand (*L'exstrophie vésicale et l'épispadias*, Paris, 1894) have, however, thrown some light upon the subject by their theory of the formation of an opening in the urogenital sinus by the breaking down of a plug of epithelial cells (the so-called "bouchon cloacal"); and Keibel (*Anat. Anz.*, vi. 186, 1891) and Berry Hart (*Trans. Edinb. Obstet. Soc.*, xxvi. 308, 1900–01) have still further elucidated the matter by showing that the bladder is really a product of the entodermal cloaca, and not (save in a small part) the result of persistence of the allantois. The development of the bladder from primitive intestine and from the part of it known as entodermal cloaca does away with many of the difficulties which stood in the way of an embryological explanation of vesical extroversion and epispadias. The entodermal cloaca is closed in front by the cloacal membrane, which at one time has no mesoblast in its composition; this cloacal membrane is believed to be derived from the margins of the blastopore or neurenteric canal, which, although primarily dorsal in position, becomes ventral by the changes in direction of growth of the caudal end of the embryo; and the imperfect formation of the cloacal membrane offers a satisfactory explanation of the various forms of vesical exstrophy and epispadias. Arrest at an early stage accounts for the cloacal forms of exstrophy; at a later stage simple extroversion of the bladder will result; and at a still later the minor degrees of exstrophy and the various types of epispadias will be produced. There are still difficulties to be explained away, but it is reasonable to hope that a further and more minute acquaintance with the ontogenesis of the caudal end of the embryo will clear them up also. In this way extroversion of the bladder falls into line with so many other malformations as essentially an arrested development.

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Urinary Umbilical Fistulæ.

A somewhat rare malformation is that in which urine flows or is expelled in a jet from the umbilicus. At the navel there is, in these cases, a granuloma or fleshy tumour, or a groove from which the fluid emerges; this represents the umbilical end of a pervious urachus communicating with the bladder cavity. The case is known as one of congenital urinary fistula of the umbilicus, or of persistent urachus, or of urachal fistula. One of the earliest known instances was that described by J. Caulton (*Gentleman's Mag. and Hist. Chron.*, xxii. 271, 1752) under the following graphic title: "Account of a negroe boy, two months old, well and thriving, who made water in a full stream from the navel as well as from the penis; the navel stream was cured by a strong solution of crude alum." Since 1752 many cases have been recorded, so that Taruffi (*op. cit.*, vii. 346, 1894) had no difficulty in collecting eighteen of them. Some of these were truly antenatal in origin, the anomaly being observed at or within a few days after birth (at the fall of the cord); others were developed in later life. The adult cases could sometimes be traced to an antenatal cause; there was evidence that a patent or easily dilated urachus existed, and that, on account of an obstruction to the normal urethra or an injury to the bladder, the new route was forced open, and so urine began to pass from the umbilicus, although it had previously been expelled by the urethra. It is not, however, with these adult cases but with the antenatal ones that we have here to do.

Of truly congenital cases Guéniot (*Bull. gén. de thérap.*, lxxxiii. 299, 348, 1872) collected seven; L. Levié (*Nederl. Tijdschr. v. Geneesk.*, 2 R., xiv. 501, 1878) increased the number to twenty-one; Naury

(*Thèse*, Paris, 1881) dealt with the treatment of the anomaly; and J. Castel (*Thèse*, Paris, 1884) brought the number of observations up to thirty-five. The full bibliography of the subject will be found in the *Index Catalogue* (Washington) under the titles *Fistula, Umbilical* (vol. iv. p. 1018, 1883; 2 s., vol. v. 837, 1900), and *Urachus, Abnormities of* (vol. xv. 39, 1894). At birth, or when the cord falls off, the infant suffering from this anomaly shows a fleshy growth at the umbilicus from which urine trickles. The growth protrudes like a hernia when the child cries or struggles; but palpation does not reveal the presence of intestine in the growth. The urethra may be closed or narrow (Rose, *Med. Rec.*, xii. 516, 1877; Charles, *Brit. Med. Journ.*, ii. for 1875, p. 486; A. Stadfeldt, *Nord. med. Ark.*, iii., No. 23, 1, 1871); but in many cases there is no obstruction, although, of course, such may have existed in antenatal life. The anomaly is more common in the male sex, possibly on account of the greater length of the urethra and the greater chance of obstruction. The essential fact in the teratogenesis of the defect is the persistence of the urachus in an open or easily opened up state; and the investigations of L. Gruget (*Thèse*, Paris, 1872) and of J. B. Wutz (*Arch. f. path. Anat.*, xcii. 387, 1883) show that this condition is occasionally found. When the umbilical end of the urachus is closed or becomes closed a cyst may develop in the abdominal wall, due to distension of the cavity of the urachus; this is called a *urachal cyst.* Many important articles have appeared dealing with such cysts, among which may be mentioned those of C. C. Wolff (*Diss. inaug.*, Marburg, 1873), of Lawson Tait (*Lancet*, ii. for 1888, p. 675), of H. Schnellenbach (*Diss. inaug.*, Bonn, 1888), and of F. B. Robinson (*Ann. Surg.*, xiv. 337, 1891). Both the fistulæ and the cysts are capable of successful surgical treatment (E. Kirmisson, *Maladies chirurgicales*, p. 224, 1898).

Miscellaneous Malformations of the Bladder.

Double or septate bladder is a rare anomaly. It has been found, however, in connection with the malformation known as diphallus or double penis (Ballantyne and Skirving, *Teratologia*, ii. 92, 184, 255, 1895). In G. Sangalli's case of diphallus in an adult (*Gazz. med. lomb.*, liii. 491, 1894) two bladders lay side by side and communicated with each other by a canal, 1 cm. long; and in M. Lange's infant (Schmidt's *Jahrb. gesammt. Med.*, ccxlv. 215, 1895) the bladder showed no sign of division externally, but internally was divided into two equal parts by a median perpendicular fold. Cases of double bladder may, however, exist apart from duplicity of the penis (Ehrlich, *Journ. compl. du dict. d. sc. méd.*, xxxvi. 24, 1830; Huppert, *Arch. d. Heilk.*, vi. 382, 1865; A. à Lebenwaldt, *Miscel. Acad. nat. curios.*, Dec. ii., Ann. viii., p. 264, 1690; F. Ferguson, *Proc. New York Path. Soc.*, p. 58, 1890). Probably most of the cases which have been described as double bladder have really been of the nature of *diverticula* of the bladder, and many instances of this latter malformation have been put on record in recent years. Among these I may mention the inaugural dissertations of C. Blumenthal (Göttingen, 1868) and L. Mitzkuner (Jena, 1878), and the articles of Bimar (*Gaz. hebd. d. sc. méd. de Montpel.*, viii. 445, 1886), J. Coats (*Glasgow Med. Journ.*, xix. 72, 1883), J. J. van Gieson (*Proc. New York Path. Soc.*, p. 171, 1888), Porter (*Dublin Quart. Journ. Med. Sc.*, xxv. 504, 1844), and F. Zachrisson (*Upsala Läkaref. Forh.*, n. F., i. 199, 1895–96). In W. Müller's specimen, a female fœtus, there was a double bladder and a uterus bicornis; the two bladder cavities were superior and inferior (*Diss. inaug.*, Marburg, 1895); and in Péan's case, a girl of fifteen years, there was an accessory bladder arising from the anterior wall of the other one, from which urine escaped by a second median urethra lying below the normal meatus urinarius (*Bull. Acad. de méd.*, p. 542, 1895). A curious case was described by F. Beach (*Trans. Path. Soc. Lond.*, xxv. 185, 1873–74) in which the bladder contained a pouch, which opened into a dilated coiled tube (a third ureter), which communicated with the right kidney by a smooth-walled cavity.

Malformations of the Kidneys.

Since the progress of surgery has brought the kidney within the sphere of the operator it has become increasingly important that he understand the anomalies of this organ. This remark applies specially to what is known as single kidney, but it has also a bearing upon all renal malformations.

Absence of both kidneys is incompatible with postnatal life of any but the shortest kind, unless indeed we accept Moulon's case (cited by H. Morris in his *Surgical Diseases of the Kidney*, p. 112, 1885) of a young girl of fourteen years as a genuine instance;[1] but it is not of extreme rarity in antenatal life, and may interfere little with antenatal growth and development. In Mayer's specimen (*Ztschr. f. Physiol.*, ii. 36, 1827), a stillborn, full-time male infant, the kidneys, ureters, urinary bladder, and renal arteries were all absent, although the heart, lungs, liver, spleen, and part of the intestines were well developed, and the suprarenal capsules were twice their normal size; the external genitals, sigmoid flexure, rectum and anus, and gall bladder were also wanting. Absence of both kidneys is not rare in sympodial monsters (*q.v.*) and in the malformed twin fœtus (acardiac, acephalic, paracephalic).

The *single kidney* appears to be a relatively frequent anomaly. Several widely different states, however, are included under this one name: these are—(1) entire absence of one kidney, or unsymmetrical kidney; (2) congenital rudimentary kidney, when one organ alone is of any functional importance; and (3) fusion of the two kidneys into one mass, the "solitary kidney," including the "horse-shoe kidney." A few words may be said about each of these types.

The unsymmetrical kidney is not very uncommon, as is borne out by the long list of references in the *Index Catalogue* (Washington) under the heading *Kidney, Abnormities of* (vol. vii. 389, 1886; 2 s., viii. 635, 1903). It may be situated in its normal position at the side of the spine, or may lie on the sacrum or in an intermediate position; it is often but not invariably of a larger size than normal; it may retain its fœtal appearance (lobulation); and it may have either a single ureter or two pelves and two ureters. When the kidney has two ureters, and more especially when these pass to opposite sides of the bladder, it may be doubted whether it is a case of unsymmetrical kidney at all; if, however, both ureters go to the same side of the bladder it is probable that it is of the unsymmetrical type. As a rule, two pelves and two ureters mean that the single kidney is really two organs fused (the "solitary" kidney).

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[1] Possibly the kidneys were misplaced and not absent.

Cases of congenital atrophy or (better) rudimentary development of one kidney are comparatively rare. Clinically, they have the same significance as complete absence. The ureter, however, is generally present in the former anomaly; and the kidney itself may be a small cystic, fibrous, or fatty mass, or may be simply small and lobulated. The ureter may be a fibrous cord, or it may have a lumen and open into the bladder, or it may be twisted on itself and have no communication with the bladder. The renal arteries and veins may show various anomalies; and, finally, the rudimentary kidney may be misplaced. Possibly some of the reported cases have been the results of antenatal or postnatal disease and are not true developmental anomalies.

The "fused kidney" is comparatively common. When both kidneys are displaced they are generally also united, but the nature and degree of the union vary much. In some instances the two organs are united at their lower ends by a thin or thick band of tissue which crosses the spine; and the single renal mass thus produced has a distinct horse-shoe shape (horse-shoe kidney). In other instances the kidneys are completely united together and form a single disc-shaped mass, with a double or a single pelvis and two ureters. Intermediate types lying between these two extremes may be met with: there may be a single S-shaped renal mass lying on one side of the vertebral column, the upper end of one kidney being united to the lower end of the other; or there may be a horse-shoe kidney, but one in which the union is more extensive than usual; or there may be a fusion of the two kidneys in such a way that the hilum of the one is joined to the outer border of the other. The fused kidney may be either lateral or central in position.

The single kidney may be found (generally by accident) in the fœtus, or it may lie unsuspected during the whole of adult life. It may, however, give rise to trouble, as when it lies in the middle line over the promontory of the sacrum, and is the cause of obstruction to delivery in women. A fatal result is produced when nephrectomy is performed and it is a single kidney that is removed; all surgeons ought, therefore, to practise catheterisation of the ureters before carrying out such an operation. G. J. Winter (*Arch. f. klin. Chir.*, lxix. 611, 1903) reports several cases (including a personal one) of surgical interference when there was a solitary kidney; his article is worthy of consultation upon this whole subject. In its clinical relations the solitary kidney is a perfect example of the teratological state whose pathological effects may be postponed till adult life or may never be revealed at all. In this respect the anomalies of the kidney have a resemblance to those of the genital organs.

Sometimes the kidneys may be normal in number but abnormal in form, and they may then be misplaced as well. Sometimes the lobulation may be very deep in the kidney at birth (as in a specimen given to me by Dr. Graham in 1894), or the fœtal degree of lobulation may persist into adult life or even into old age (L. L. M'Arthur, *Ann. Surg.*, xxxiv. 203, 1901). A kidney may show two pelves and one ureter or two pelves and two ureters; the hilum may be absent; or the ureter may lie in front of instead of behind the renal artery and vein at the hilum. Anomalies of the renal arteries have also been noted, either in association with other malformations or alone; the most common anomaly is the presence of more than the usual number of arteries (Micheleau, *Journ. de méd. de Bordeaux,* xxviii. 188, 357, 445, 487, 1898; xxix. 39, 1899), and the supernumerary ones may arise from the aorta, or the lumbar, suprarenal, iliac, or middle sacral arteries. A "floating" kidney possesses a mesonephron and abnormally long vessels; it is due, therefore, to an antenatal anomaly of the peritoneum. Rarely the kidneys are increased in number to three (J. Hyrtl, *Oesterr. med. Wchnschr.*, 965, 1841) or four (M. L. Amick, *Cincin. Med. Repert.*, iv. 551, 1871).

The various anomalies of the kidney are apt to be associated with malformations of other organs, among which must be specially mentioned the genital organs and the anus. There may, for instance, be atresia ani (B. Langenbeck, *Deutsche Klinik,* x. 77, 1858), or a bicornate uterus (S. H. Scheiber, *Med. Jahrb.*, 260, 1875), or a unicornate uterus (F. C. Turner, *Trans. Path. Soc. Lond.*, xxxvii. 284, 1885–86).

"Cystic" kidney is hardly to be regarded as an embryonic malformation; indeed I have already considered it in the first volume of this MANUAL among the fœtal diseases (p. 383). It has, also, been regarded as a neoplasm. I have recently met with a case of labour in which a large cystic kidney on the left side was the cause of great delay (specimen No. 327 in my list); in this instance there was also hypospadias. Similar cases have been reported by Gailleton and Ollier (*Gaz. d. hôp.*, xxvi. 433, 1853), Porak (*France méd.*, ii. for 1885, p. 1441), C. W. F. Uhde (*Monatschr. f. Geburtsk. u. Frauenkr.*, viii. 26, 1856), and W. Wolff (*Berl. klin. Wchnschr.*, iii. 269, 1866; iv. 480, 1867).

In describing renal anomalies I have referred also to *malformations of the ureters* (absence, duplication); but I may further note here that cases of apparent low termination of these canals have been observed by F. Colzi (*Sperimentale, Sez. biol.*, p. 37, 1895), A. Wölfler (*Prag. med. Wchnschr.*, xx. 231, 253, 1895), and others. The ureters opened in the vestibule a little below the normal meatus urinarius, the patients being women. D. Berry Hart (*Trans. Edinb. Obstet. Soc.*, xxvi. 313, 1901) does not think that the tubes which thus open so low down are altogether ureters; he regards them as due to persistence of the Wolffian duct and of the original communication between it and the ureter. Incontinence of urine is the clinical feature in this anomaly. Somewhat analogous cases are met with in the male subject, when the ureter opens into the vas deferens or seminal vesicles (Tangl, *Arch. f. path. Anat.*, cxviii. 414, 1889). For a list of references to the literature of ureteric malformations the reader may again consult the invaluable *Index Catalogue* (vol. xv. p. 53, 1894).

Malformations of the Penis.

Complete *absence of the penis* is very rare save in combination with such grave monstrosities as sympodia and acephaly. In 1897, however, I received a letter from Dr. R. P. Harris of Philadelphia in which he told me of two cases in adults which he had met with in Philadelphia. Dr. Harris afterwards published these two instances (*Phila. Med. Journ.*, i. 71, 1898), and gave a summary of five others (those reported by Goschler, Rauber, Nelaton, Mathews, and Collier), drawing the conclusion that there is one male infant born with this defect in about 30,000,000. The rarity of complete absence of the penis is in striking contrast with the frequency of rudimentary development (as in extroversion of the bladder, hypospadias, etc.). In five of the seven cases collected by Harris the urine was passed into the rectum apparently by an opening in the anterior rectal wall, and in the other two the urethra opened in the perineum just outside the anus. J. Bloomfield's patient, a man, thirty-five years of age, was a twin (*Columbus Med. Journ.*, p. 133, 1895); so was Lemke's infant (*Arch. f. path. Anat.*, cxxxii. 181). In all the instances cited, there was a scrotum containing testicles, and the characters of the individual were distinctly male. The urine did not cause much irritation in the rectum unless the individual happened to develop hæmorrhoids; it was this fact that suggested to surgeons the possibility of turning the ureters into the bowel in cases of ectopia vesicæ, a proceeding the feasibility of which was experimentally determined by R. H. Reed (*Ann. Surg.*, xvi. 193, 1892).

Duplication of the penis or *diphallus* is one of the teratological states that lie on the border line between the single or monosomatous terata and the double or polysomatous terata. When the double penis is associated with one or two supernumerary lower limbs the case is by everyone regarded as belonging to the double terata or united twins; but when diphallus is the solitary external anomaly it becomes much more difficult of classification and is obviously one of those connecting links which are so disturbing to all systems of classification.

In 1895 Dr. Scot Skirving and I described an instance of diphallus in the tenth child of healthy parents (*Teratologia*, ii. 92, 1895). The scrotum was divided into two lateral lobes by a deep groove in the middle line, and these lobes merged together in the middle line anteriorly but were quite distinct posteriorly (Fig. 80). Each of the scrotal pouches contained an apparently normal testicle. In the middle line of the perineum was an ill-defined swelling from which two short but perfectly recognisable penes arose; each of them had a prepuce so short as to expose the whole glans; and each had a meatus urinarius, but that on the left side appeared to end blindly. Behind the penes and in front of the anus (which was normal), there was an area in which the skin was defective; in the centre of this was a mound of red, ill-formed material, apparently granulation tissue (*k* in Fig. 80), and on each side, between it and the healthy skin, was a groove or sulcus (*g*, *h* in Fig. 80). During the act of micturition, a gush of urine came from the centre of the granulation mass (urinary fistula), while at the same time a few drops came from the right meatus urinarius.

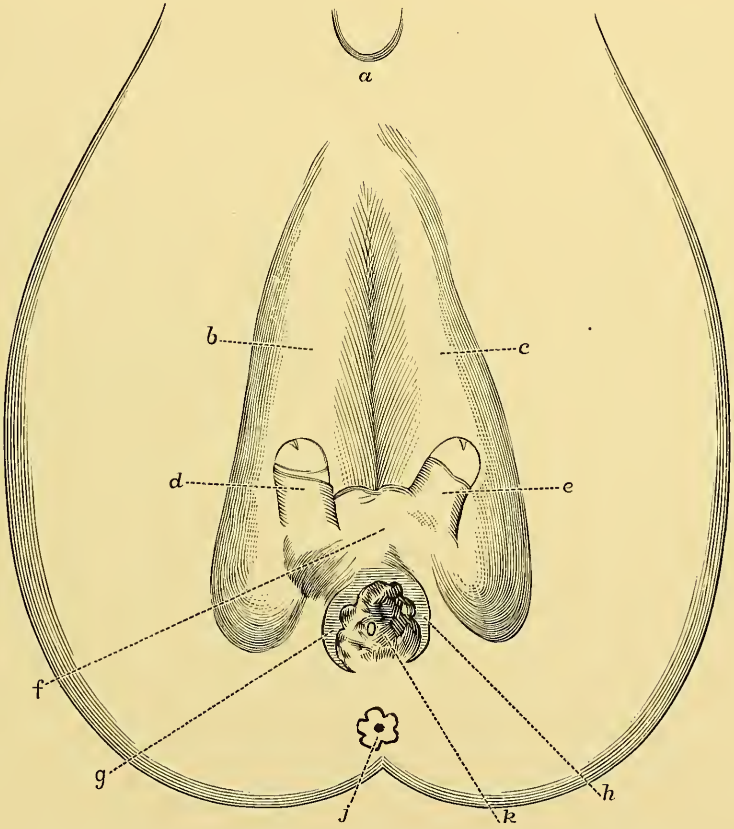

Fig. 80.—Sketch of Genital Organs in Case of Diphallus, with Infant in Lithotomy Position (Case No. 137).

a, symphysis pubis; *b*, *c*, right and left halves of scrotum; *d*, *e*, right and left penises; *f*, common swelling at root of penises; *k*, granulation mass, with urinary fistula in centre, and sulci at each side (*g*, *h*); *j*, normal anus.

I have elsewhere (*Teratologia*, ii. 182, 255, 1895) gathered together the literature of diphallus up to the year 1895, finding records of twenty observations in all; but since then a few more instances have

been reported (H. Küttner, *Beitr. z. klin. Chir.*, xv. 364, 1896; M. Lange, *Beitr. z. path. Anat. u. allg. Path.*, xxiv. 223, 1898; J. H. Morgan, *Trans. Clin. Soc. Lond.*, xxix. 216, 1896; Hofmokl, *Wien. med. Presse*, xxxvii. 1396, 1896; *Arch. f. klin. Chir.*, liv. 220, 1897; F. Neugebauer, *Gaz. lek.*, 2 s., xvii. 561, 1897, *Pam. Towarz. lek.*, xciii. 327, 1897, *Centrlbl. f. Gynäk.*, xxvi. 1395, 1902). One of the most interesting and typical cases was that described by Jenisch (*Med. Cor.-Bl. d. württemb. ärztl. Ver.*, vii. 129, 1837). The patient was a full-time male infant, well formed save in the following details. In place of one penis there were two, situated near to each other, of which one (the right) had the appearance and size of that of a normal infant, while the other (the left) was larger and was not furnished with a prepuce. Each penis had a patent urethra, from which urine along with a trace of meconium was expelled; each had its own scrotum, but each scrotum contained only one testicle (Fig. 81). Behind the scrotal sacs was an elevation made up of spongy folds of

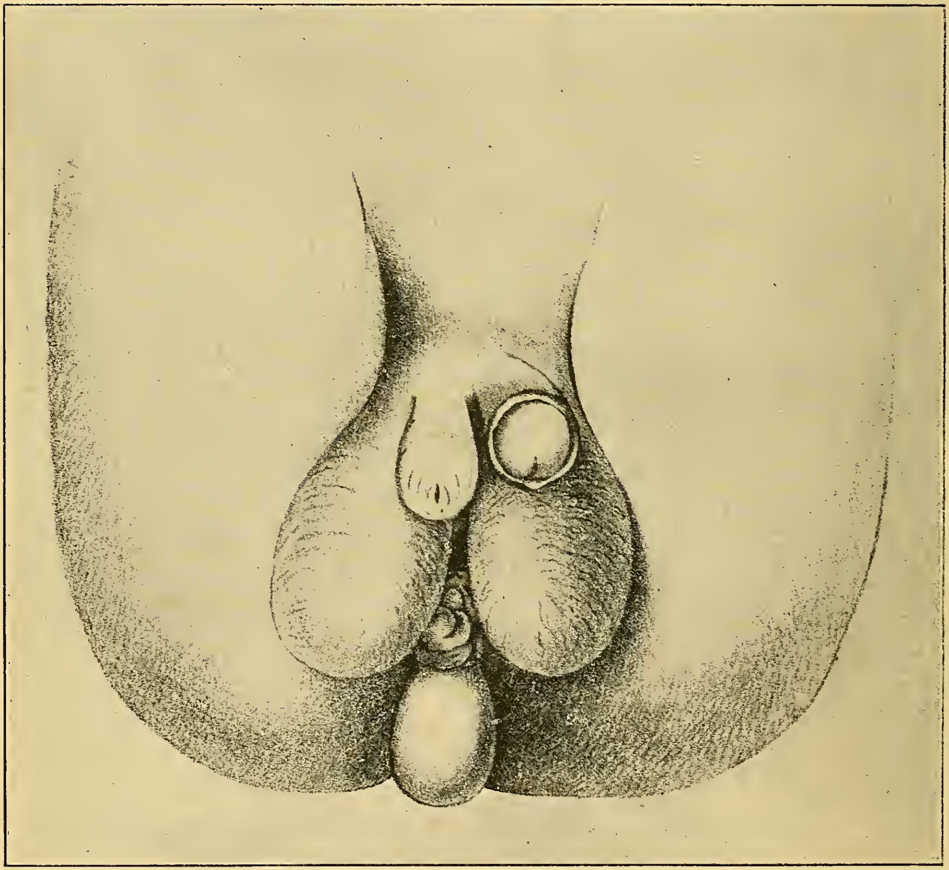

FIG. 81.—Case of Double Penis (Diphallus).

skin darker in colour than the surrounding integument; near to this was attached a steatomatous tumour in the position of the absent anus. A sound could be passed through both urethræ into the bladder, and thence through an opening in the posterior wall of the neck of that viscus into a cavity behind it (the intestine). The atresia ani was operated on unsuccessfully, and the infant died.

In the article to which I have referred (*Teratologia*, ii. 92, 184, 255, 1895) considerable attention was paid to the clinical history and morbid anatomy of the recorded cases of diphallus, and it is unnecessary to repeat the details here. It may, however, be stated that the malformation of the penis did not in itself interfere with postnatal life, although it was usually productive of sterility (physiological incompetence). Generally the two penes were situated close together; but in a few instances they were widely separate, recalling the double genital tubercles of the specimen of gastroschisis shown in Fig. 79 (p. 544); the two penes may be so close together as to justify the term bifid or bifurcated penis. In a few instances the bladder appears to have been double, or at least consisted of two compartments; and in one case, at least, there were said to be three testicles. In a number of the records it was stated that the anus was imperforate or opened in an abnormal situation. From the point of view of teratogenesis it is unfortunate that little is known regarding the state of the lower end of the spine in diphallus; but in some instances there was unusual breadth of the pelvis, pointing to some tendency to duplication of the sacrum. In Pigné's case (*Bull. Soc. anat. de Paris,* xxi. 110, 1846), an anencephalic fœtus, there were two stomachs, two pericardial sacs (each containing a well-formed heart), four lungs, and two aortæ; yet the fœtus was externally single save for the presence of two penes. The symphysis pubis may be defective and the lower limbs shorter than normal.

The diphallic monstrosity presents problems of the greatest difficulty when we try to classify it or to explain its origin and nature. With regard to classification, it would seem to be best to look upon it as a slight form of duplication of the fœtus, and to consider it (as Taruffi does, *Sull'ordinamento della teratologia*, Bologna, 1896, 1898) as really two pelves joined together, so that each ilium represents one pelvis and the sacrum is really two fused together. Taruffi admits the hypothetical nature of this view; and, of course, if it had been well established I should have placed diphallus with the polysomatous terata and not with the monosomatous. As it is, I retain the type among the single monsters just as I did polymastia and some other malformations by excess. At the same time I am inclined to accept Taruffi's hypothesis, especially as two penises are actually met with in cases of undoubted double monster, such as the tripod (three-legged) monstrosity exemplified in Jean Battista dos Santos (W. Acton, *Med.-Chir. Trans.*, Lond., xxix. 103, 1845–46; E. Hart, *Lancet,* ii. for 1865, p. 124; P. D. Handyside, *Edinb. Med. Journ.*, xi. 833, 1866). I do not, however, regard it as advisable to adopt Taruffi's name ("Syncephalus dilecanus dipleurus dipus"), and retain the shorter "diphallus." It is only fair to state that, instead of regarding this monstrosity as a minimum degree of duplication of the individual, it is competent to look upon it as a reversion to a lower type, for a double penis is a character of some of the lower animals. Yet another view is possible, namely, that the penis is developed from the fusion of two lateral genital tubercles, and that, therefore, diphallus represents an arrested development, each penis being really only a half organ.

Duplication of the urethra in the penis has been observed by J. Englisch (*Wien. med. Presse*, xxix. 985, 1888) and others (J. Wood, *Trans. Path. Soc. Lond.*, x. 201, 1858–59); and three urethræ in one glans penis were noted by Szymanowski (*Vrtljschr. f. d. prakt. Heilk.*, lxxxiii. 23, 1864). Various anomalous canals may also be met with in the penis, which communicate neither with the urethra nor with the ejaculatory ducts; or there may be diverticula of the urethra itself; or, finally, there may be fistulæ extending from the rectum to the urethra and opening into it (usually in cases of atresia ani). All these varieties of penile canals are described by C. Taruffi in his work entitled *Sui canali anomali del pene*, Bologna, 1891. Perhaps some of these canals are due to incomplete antenatal cure of epispadias. Some years ago Dr. W. Fordyce published in my journal (*Teratologia*, i. p. 61, 1894) a case of fœtal ascites in which there was a curious penis-like body (Fig. 82); this body, on transverse

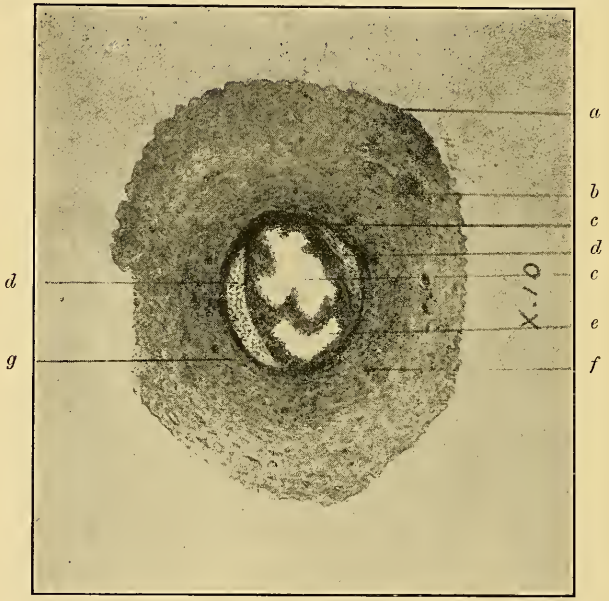

Fig. 82.—Transverse Section of Penis-like Body, × 10, in case of Fœtal Ascites.

a, skin surface; *b*, connective tissue; *c*, unstriped muscle; *d*, cavernous erectile tissue; *e*, canals lined by cubical epithelium; *f*, nerve in section; *g*, area of denser connective tissue.

section, showed two canals, which communicated not with the bladder, but with two canals (vaginal ?) which passed to two uterine horns. The exact nature of the penis-like body is doubtful, but Fordyce regarded it as the united labia minora containing the hypertrophied and irregularly developed clitoris.

Various degrees of *atresia of the urethra* in its course through the penis have been recorded. In some of these the bladder became greatly distended with urine in antenatal life (*vide* Vol. I. of this Manual, pp. 379–382). Sometimes the obstruction is valvular, and then a diverticulum of the urethra may be developed behind it, giving rise to the curious penile pouches described in detail by Johann v. Bokay (*Jahrb. f. Kinderhlk.*, 3 F., ii. 181, 1900) and others (*e.g.* S. Grosglik, *Monatsber. f. Urologie*, vi. 577, 1901). *Congenital phimosis* is an anomaly so well known and so frequently and so fully described that I need do no more than mention it here. *Absence of the prepuce* at birth has also been reported (M. Roth, *Cor.-Bl. f. schweiz. Aerzte*, xiv. 441, 1884), sometimes in association with occlusion of the meatus urinarius (H. J. Garrigues, *Amer. Journ. Obstet.*, xii. 615, 1879). Numerous references to articles on these various anomalies of the male urethra are to be found in the *Index Catalogue* (Washington), vol. xv. 57, 1894.

Epispadias is a well-known malformation of the penis. Through the presence of a groove or fissure of varying extent the urethra is laid open along the dorsum of the penis. It is most commonly associated with extroversion of the bladder, being indeed very rare as a single malformation. E. Kirmisson (*Maladies chirurgicales*, p. 282, 1898) has reported and figured two typical cases, and others are to be found in the list of references in the *Index Catalogue* (vol. iv. 306, 1883; 2 s., vol. v. 84, 1900); but it is of much less frequent occurrence than hypospadias. Sometimes the fissure affects the whole penile urethra; in other (very rare) cases the glans alone is affected (balanic epispadias). The penis itself is generally small in size, and the prepuce is well marked on the lower aspect. Such malformed individuals often survive birth, and may, as F. Mayr has shown (*Diss. inaug.*, München, 1892), belong to the criminal class; there may or may not be incontinence of urine, and impotence is common. The teratogenesis of epispadias is probably the same as that of extroversion of the bladder, namely, breaking down or arrested formation of the cloacal membrane in the lower part of its extent. Epispadias may be surgically corrected either by the procedure of Thiersch or of Duplay (*vide* A. Zöller (*Diss. inaug.*, Heidelberg, 1893), C. Bayer (*Centrlbl. f. Kinderh.*, iii. 1, 1898), and others).

Hypospadias (the presence of a groove along the lower aspect of the penis opening into the urethra) is comparatively common. I have met with it in a number of cases, two of which I have published (*Teratologia*, i. 95, 1894; ii. 119, 1895). The male urethra may be divided into three parts, which may be named membrano-prostatic, spongy, and balanic or glandular. When the canal is not closed in at all anterior to its membrano-prostatic part, the hypospadias may be called *perineal* or *scrotal*; this is the most severe form of the deformity; and it constitutes a comparatively common type of *pseudo-hermaphroditism*, for the scrotum is usually cleft and the testicles have often failed to descend. When the deficiency in the lower urethral wall exists somewhere in the spongy portion, the *penile* variety results; and when it is in the glandular portion we have to do with the *balanic* or *glandular* form. Intermediate types also exist, such as F. C. Schaefer's, in which the hypospadias was partly of the penile and partly of the scrotal type (*Chicago Clin. Rev.*, p. 434, 1894). In the balanic form the urethra, instead of opening in its normal position, does so at the base of the glans; various minor varieties of it may exist, as where the meatus urinarius is found in its normal place, but leads into nothing more than a cul-de-sac. A good description of the minor varieties of all the three leading types of hypospadias is given by C. Kaufmann (*Verletzungen und Krankheiten der männlichen Harnröhre und des Penis*, Stuttgart, 1886). Associated malformations, such as flattening of the glans, torsion of the penis, atrophy of corpus spongiosum, atresia ani, non-descent of the testicles, webbed penis, and a pseudo-vulvar orifice, are not uncommonly met with. Hypospadias, also, may show family prevalence, two or more brothers in the same family being affected with it, as in T. H. Kellock's observation (*Trans. Clin. Soc. Lond.*, xxxii. 242, 1898–99), and in several other instances which have been carefully collected by F. Neugebauer (*Monatschr. f. Geburtsh. u. Gynæk.*, xv. 281, 1902). Hereditary transmission has also been noted (E. Lesser, *Arch. f. path. Anat.*, cxvi. 537, 1889). There may be incontinence of urine, but commonly there is only the inconvenience arising from the abnormal direction in which the urine flows. Sterility is common, but nor constant, as Dombrovski's case shows (*Vrach. Gaz.*, St. Petersburg, viii. 962, 1901). The mode of production of hypospadias is arrested closure of the groove along the under surface of the genital tubercle, and E. Loumeau (*Arch. prov. de chir.*, iii. 320, 1894; *Journ. de méd. de Bordeaux*, xxiv. 121, 1894) has shown how different minor varieties are accounted for by arrested development at different stages. The anomaly may be met with in the lower animals, as in the dog (Retterer et Roger, *Journ. de l'anat. et physiol.*, xxv. 113, 1889). Treatment, which is almost of necessity surgical, may consist solely in separating the penis from its fixed position (as in webbing of it to the scrotum), or may be of the nature of a separate operation. In the latter case the reconstruction of the urethra may require to be performed by successive operations. The literature of hypospadias, somewhat extensive, is to be found in the *Index Catalogue* (vol. vi. 747, 1885; 2 s., vol. vii. 770, 1902).

I have only space to name some other malformations of the penis: such are webbing of it whereby it is enclosed in the skin of the scrotum (P. Strassmann, *Ztschr. f. Geburtsh. u. Gynäk.*, xxviii. 183, 1894); a supernumerary glans penis (Daunic, *Arch. prov. de chir.*, i. 518, 1894); shortness of the frænum (C. Féré, *Rev. de chir.*, p. 333, April 10, 1895); and that very rare anomaly, antenatal paraphimosis (P. Strassmann, *Ztschr. f. Geburtsh. u. Gynäk.*, xxviii. 181, 1894). An individual with a vulva and a pseudo-penis lying posterior to it (implanted on the perineum) was described by F. Neugebauer in 1899 (*Centrlbl. f. Gynäk.*, xxiii. 139, 1899); I know of no other modern instance like this.

Anomalies of the Testicles.

A few sentences must suffice for a description of testicular anomalies. The commonest is *displacement* or *ectopia*: this is generally due simply to non-descent of the testicles, and is therefore fœtal rather than embryonic in origin; it may, however, be due to causes which are embryonic. The missing glands may be either in the abdomen or in the inguinal canals; rarely is a testicle found displaced into the perineum (Hoeck, *Centrlbl. f. Gynäk.*, xviii. 99, 1894). When one testicle alone is absent from the scrotum, the individual is called a *monorchid*, although it is more than probable that he really possesses both testicles; when both testicles are displaced, he is called a *cryptorchid*, and this name more truly expresses the state of matters. Monorchids may be sterile; cryptorchids are almost of necessity so, for it would appear that the testicle does not usually produce spermatozoa until it reaches the scrotum, although it may influence the growth of the body at puberty (J. Griffiths, *Journ. Anat. and Physiol.*, xxviii. 209, 1894; W. M. Eccles, *Brit. Med. Journ.*, i. for 1902, pp. 503, 570).

Anorchidy or true absence of the testicles is a very rare teratological state; probably most of the recorded cases were instances of rudimentary development of the glands and non-descent. Both testicles may be found in one half of the scrotum (*ectopia testis transversa*), as in the case of the eight years old boy seen by M. Jordan (*Deutsche med. Wchnschr.*, xxi. 525, 1895). Fusion of the testicles (*synorchidy*) may be abdominal or scrotal; it has been regarded as an atavistic phenomenon, the condition being normally found in some of the lower animals; it is very rare in the human subject. Increase in the number of testicles (*e.g. triorchidy*) has occasionally been reported, and some references may be found in the *Index Catalogue* (vol. xiv. 319, 1893); but it is always doubtful whether the supernumerary glands are really testicular in nature, unless an autopsy and microscopical examination can be made. F. Parona's case of several testicles in the scrotum (*polyorchidy*) is a most anomalous one (*Policlinico*, iii. 203, 1896).

Before I leave the anomalies of the testicle, I must refer to the frequency of the development of malignant disease in the misplaced testicle in later life; to the association of this abnormity with congenital hernia; to the hereditary transmission of ectopia testis; and to the enlargement of the mammary glands (*gynæcomastia*) in later life, when the testicles are abnormal and the individual is also a hypospadiac.

Malformations of the Female Genitals.

The anomalies of the genital organs in the female form a large and important group; but although most of them are developed in embryonic or in early fœtal life they have little or no effect on the physiology of the individual until late in postnatal life. In fact, if the woman never become pregnant most of her genital anomalies are never discovered at all, or are only accidentally revealed. The genital anomalies, therefore, are good examples of the postponed effects of antenatal morbid states. For this reason we find very full accounts of them in the text-books of Gynecology and Obstetrics, and for the same reason I do not intend to discuss them in detail in this work. Those of my readers, however, who may wish to obtain such detailed knowledge will find my articles in Allbutt and Playfair's *System of Gynæcology* (pp. 63–112, 1896) and in Reed's *Text-Book of Gynecology* (pp. 118, 131, 274, 473, 560, 1901, 2nd edit., 1904) sufficiently full to open up the subject to them. I shall content myself here with some general remarks.

In the first place, the anomalies of the female genitals have the peculiarity that some of them are produced comparatively late in antenatal life and some in postnatal existence. The reason is to be found in the late development of the genital organs. While some of the ontogenetic processes are finished in the early weeks during the embryonic stage, others are long delayed and are perhaps only completed some years after birth. For instance, the development of a well-marked fundus for the uterus only takes place at puberty, and the absence of such a fundus, leading to the anomaly known as the *uterus infantilis* or *planifundalis*, is, therefore, a morbid state which arises far on in postnatal existence. Again, the septum between the two halves of the uterus may be found as late as the fifth month of antenatal life; if, then, part of this septum persist, producing the anomaly known as the *septate uterus*, the date of production of this anomaly may be regarded as the fourth or fifth month. A little earlier in antenatal life there are external indications of the double state of the uterus in the presence of two horns or cornua; an arrested development at this stage (third or fourth month) produces the *uterus bicornis* or bicorn uterus. Still earlier, the two halves of the uterus are quite separate, and if they remain so the anomaly known as the *uterus duplex* or *uterus didelphys* is formed, or if, still earlier, one of the two halves fail to appear at all, the *uterus unicornis* results. Finally, failure of both halves of the uterus (Müllerian ducts) to develop is a very early anomaly, and gives rise to absence of the organ (*defectus uteri*) or to a very rudimentary state of it (*uterus rudimentarius, membranaceus*, etc.). It is evident, therefore, that the uterine anomalies (and the same might be said of the vaginal and tubal and vulvar) originate at various times in antenatal and postnatal life; they may be embryonic, fœtal, or infantile in their teratogenesis. In this respect they differ from most of the malformations described in this volume, for the latter are embryonic in the time of their production.

In the second place, most of the anomalies of the female genital organs very obviously are arrested developments. The embryological theory of teratogenesis explains them satisfactorily and as a rule completely. This has been shown conclusively by many writers, among whom F. von Winckel deserves special mention (*Ueber die Eintheilung, Entstehung und Benennung der Bildungshemmungen der weiblichen Sexualorgane,* Leipzig, 1899). Now and again, as in the case of the *trifid uterus, female epispadias,* and *atresia ani vaginalis,* we meet with teratological states which are with difficulty ascribed to arrested development; but in most of these instances evidence is not wanting that if we had a more perfect knowledge of the early embryological phenomena of the formation of the genitals, and more especially of the formation of the associated urinary and alimentary systems, we should have little trouble in satisfactorily explaining them all. Thus, in *vaginal and hymeneal anomalies* it is clear that there are facts not explicable on the hypothesis that the vagina and hymen are developed solely from the ducts of Müller, but which become capable of explanation if the theory of origin of the canal from the lower ends of the Wolffian ducts (D. Berry Hart, *Trans. Edinb. Obstet. Soc.,* xxii. 18, 1897) be accepted. *Hypospadias* in women is not comparable to the anomaly of the same name in the male sex; for it really represents a persistence of the urogenital sinus; in this malformation the urethra appears to open into the vagina at a higher level than usual.

Since I wrote the articles on malformations of the female genitals to which reference has been made, I have met with a variety of anomaly quite new to me and of which I can find no notice in literature. It was the case of a girl, two years of age, whom I saw in December 1899 in Professor Annandale's Ward in the Edinburgh Royal Infirmary. The anomaly consisted in a *congenital deficiency of the perineum,* with some prolapse of the rectal wall anteriorly and on the left side. Had there existed a vulvar anus the condition would not have been so peculiarly anomalous; but fæces were passed through the anal opening lying behind the rudimentary perineum. The hymen had the usual pouting form seen in the infant, and there was no spina bifida and no other malformation. At first I thought the child might have been born as a breech presentation and have had the perineum torn accidentally; but there was no history of anything of the kind having occurred. The case is No. 241 in my list.

Malformations of the Anus and Rectum.

Stenosis of the rectum and anus is comparatively rare, although possibly it sometimes escapes notice and undergoes natural cure by dilatation. It may consist simply in slight narrowness which is first noticed when the child begins to pass solid fæces; or it may be very marked and give trouble soon after birth. In the latter case the anal aperture may be occluded by a hymen-like membrane with a tiny opening in it. In other instances a valvular obstruction may exist in the rectum above the anus. A curious form of obstruction which may be classified with the cases of stenosis is that in which a cutaneous band bridges over the anal aperture passing from the skin over the coccyx to the perineum (J. H. Morgan, *Lancet,* ii. for 1881, p. 705). Such forms of malformation are capable of successful surgical treatment (dilatation, incision, excision).

Imperforation or complete occlusion of the anus or rectum or both is more common. A thin membrane may entirely close the anus; or there may be no indication at all of the anus or of the lower part of the rectum; or, again, the anal opening may be present but the rectum may be absent higher up. I have met with several instances of these anomalies. To one of these I may specially refer as it was of a somewhat unusual kind. It occurred in a 5½-months male fœtus, the product of the fourteenth pregnancy of a healthy woman, who had, however, had three miscarriages. There was no external indication of an anus, but a marked postanal dimple existed; the internal organs of the fœtus showed no abnormality save that the greater part of the large intestine was contracted and that the rectum ended blindly at a distance of 1 cm. from the perineum, its terminal cul-de-sac being in close contact with the posterior surface of the urethra at its point of origin from the bladder (*Trans. Edinb. Obstet. Soc.*, xix. 49, 1894). Differences exist as to the level at which the intestine ends, a fact which the surgeon must keep constantly before him in his efforts to relieve those abnormalities by operative procedures.

Abnormal terminations of the rectum are occasionally met with, and show many differences, chiefly as regards position. In some instances the bowel ends on the skin surface at the root of the penis, behind the scrotum, at the symphysis pubis, in the gluteal region, in the loin, or through an opening in the sacrum. In other instances the bowel may end in one or other of the surrounding mucous canals or viscera. Thus there may be *atresia ani vesicalis,* a narrow canal passing from the rectum to open into the bladder near the trigone or at the fundus; there may be the closely allied *atresia ani urethralis,* in which the bowel communicates with the male urethra, usually in its membranous portion; there may be *atresia ani vaginalis* or *vulvar anus,* in which the rectum empties itself by an opening immediately within the fourchette; or, finally, there may be the extremely rare form in which the rectum has a communication with the vaginal canal high up.

Many of these rectal and anal anomalies can be explained by the embryological theory of teratogenesis, and had we a more perfect acquaintance with all the details of the ontogenesis of the caudal end of the embryo we should, I believe, be able to account for them all, even for the most anomalous of them. I need hardly say that the ingenuity of surgeons has for long been exercised in the treatment of these defects, and with no small measure of success.

The *literature* of the subject is very large, and the reader is referred to the *Index Catalogue* of Washington (vol. i. 460, 1880; vol. xi. 1054, 1890; 2 s., i. 559, 1896).

Hermaphroditism.

In treatises on teratology much space is commonly given to the consideration of hermaphroditism and pseudo-hermaphroditism. Isidore G. Saint-Hilaire, for instance, in his *Histoire des anomalies*

(ii. 30–173, 1836) gave 143 pages to the discussion of the subject. This work, however, is not a treatise upon teratology but a book dealing with antenatal pathology, and there is a difference between the two things. Nearly all the importance of hermaphroditism is centred in its postnatal phenomena : there is the matter of registration of the infant, there is the social and political position of individuals of doubtful sex, and there are numerous medico-legal questions, such as nullity of marriage and the like, which may arise in any given case. These, however, all are the postponed effects of antenatal morbid states; they are due to states which do not themselves interfere with antenatal life and health. Such phenomena are of the greatest interest, and involve problems not easy of settlement; but, at the same time, from the standpoint of antenatal pathology, they have just the same degree of importance as attaches to the fact that a man with deformed fingers may be incapable of performing certain manipulations, such as playing the piano or firing a gun. We have to study their characters and mode of origin at and before birth; but with the complications and consequences which are set up by them in adult life we have not specially to do. In this way the subject of hermaphroditism is, for the antenatal pathologist, considerably narrowed.

Let us consider in the first place what is the antenatal aspect of *pseudo-hermaphroditism.* This morbid state is due to the existence of a malformation of either the male or the female organs of generation; this is the essential fact from the antenatal pathologist's standpoint. This malformation may lead to the individual who is really a malformed male being brought up as a girl; he may thus acquire feminine habits and possibly some of the secondary sexual characters of the female may appear; but true menstruation does not occur, and so an anomalous condition arises in which there is a certain degree of mixture of the characters of both sexes, often with troublesome and even tragic results. Still the individual is just what he or she was at first—a malformed male or a malformed female. To the former case, that in which testicles are present, the name of *pseudo-hermaphroditismus masculinus* or *androgyny* is given; the latter, in which ovaries are in existence, is called *pseudo-hermaphroditismus femininus* or *gynandry.*

One form of androgyny is that in which the testicles have not descended into the scrotum at the time of birth; since the penis may remain small at puberty while the breasts may enlarge, it is easy to understand how doubts as to the proper sex of the individual may arise. The essential antenatal fact, however, is the want of descent of the testicles. Again, the condition of hypospadias (penile or scrotal) may be present at birth, with the result that the child is registered as a girl and brought up as such; in this instance there may be a trace of a uterus and the mammæ may enlarge (gynæcomastia) and a pseudo-vulva be formed. Nevertheless, the individual is nothing more than a hypospadiac male, and the antenatal phenomena are simply the existence of a defective penis (hypospadias) and the persistence (in a male) of the parts of the Müllerian ducts which form the uterus (in the female).

In gynandry the ovaries are present, but some malformation obscures the true sex. The clitoris, for instance, may be enlarged, and the labia united behind it (atresia vulvæ superficialis); or there may be a single or a double inguinal ovarian hernia, simulating descent of the testicle; or, at a later date, hair may develop on the face. In these instances, the individual although really a female, takes on some masculine characters; but, again, from the antenatal standpoint the case is one of embryonic or fœtal malformation.

The early writers dealt with another form of pseudo-hermaphroditism, that in which the external organs of both sexes were present. Modern teratologists have been inclined to doubt the correctness of the old observations; but I think the old authors were not wrong in their descriptions, they were only in error in their interpretation of them. I believe the cases were of the same nature as those reported in recent years by Moostakov (*Meditzina*, i. 32, 1894; abstract in *Teratologia*, ii. 234, 1895) and by Neugebauer (*Monatschr. f. Geburtsh. u. Gynæk.*, vii. 550, 1898); they were in other words instances either of diphallus or of double vulva. In the former case one of the penes was probably hypospadiac and so caused the appearance of the two sexes; while in the other, one vulva might be closed and its clitoris enlarged so as to produce the same effect. The antenatal aspect of the subject is the fact that two penes or two vulvæ[1] may exist in an individual who is otherwise single, and that one of them may be so malformed as to resemble the organ of the opposite sex.

Besides these cases of pseudo-hermaphroditism which are, after all, simply antenatal malformations, there are also some recorded instances which have been classed as *true hermaphroditism*, and which are of a quite peculiar nature. They are the cases in which the essential reproductive organs of both sexes (ovaries and testicles) are present in the same individual. Of the *bilateral* form of true hermaphroditism (that in which an ovary *and* a testicle are present on both sides of the body), no absolutely conclusive example in the human subject has yet been recorded; C. L. Heppner's case (*Arch. f. Anat. Physiol. u. wissensch. Med.*, 679, 1870; *St. Petersb. med. Ztschr.*, n.s., iii. 87, 1872), in which there was a rudimentary uterus and vagina, and, on both sides, a normal ovary, parovarium, and tube, with near to each ovary a body resembling a testis, may have been a genuine instance; but the complete identification of the bodies near the ovaries with testicles cannot be regarded as accomplished. *Lateral* hermaphroditism, in which there is an ovary on one side and a testis on the other, has been occasionally reported as in the cases of Schmorl (*Arch. f. path. Anat.*, cxiii. 229, 1888) and Obolonsky (*Ztschr. f. Heilk.*, ix. 211, 1888). *Unilateral* hermaphroditism is that state in which there is an ovary *or* testis on one side and an ovary *and* testis on the other. Blacker and Lawrence (*Trans. Obstet. Soc. Lond.*, xxxviii. 265, 1896) have reported such a case: the fœtus possessed a uterus unicornis, a normal ovary and tube on the right side, and on the left side an ovo-testis, with a vas deferens and epididymis. The left sexual gland (ovo-testis) in one part showed cell columns, cell nests, and Graafian follicles with a large quantity of stroma (ovarian portion); and in a second part exhibited an abundant stroma, with definite tubules filled with cells, and forming at the hilum a rete-like structure (testicular portion). In 1901 I received for examination a fœtus with hypospadias, which one of my students, Charles R. Whittaker, dissected for me. Besides finding various muscular and vascular anomalies in different parts of the body, Mr. Whittaker found a testicle and an ovary on the right side and an ovary (with tube) alone on the left side.

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[1] As in J. Suppiger's case (*Cor. Bl. f. schweiz. Aerzte*, vi. 418, 1867; viii. 744, 1878) and in G. Chiarleoni's (*Ann. di ostet.*, xvi. 469, 1894).

The foregoing cases prove that anatomical hermaphroditism exists in the human subject; but there is as yet no evidence that in one individual two functionally active glands of the opposite sexes can exist. We need not, therefore, consider physiological hermaphroditism; but anatomical hermaphroditism presents us with a practically insoluble problem. It cannot be explained on the theory of arrested development; at least I can think of no way in which to account for the facts on such a hypothesis. It is, of course, open for us to regard such cases as instances of fusion of two individuals, one male and the other female, the fusion being so complete that only the left genital gland of the one and the right of the other have been left to give a hint that such a fusion has taken place. But this theory is not available until twins in the same amnion and of different sexes have been met with, or until united twins of different sexes have been clearly proved to exist. If, again, we maintain that the genital glands are originally neuter and that one may develop into an ovary and the other into a testicle, then we are met by the difficulty of the cases in which an ovary and a testicle have been found on the same side of the body. The only other explanation which seems feasible is to regard hermaphroditism as a phenomenon of the germinal period of life, as a reversion to a lower form of animal construction; this, it need hardly be added, is a most unsatisfactory view.

Literature.—References to articles bearing on hermaphroditism and pseudo-hermaphroditism are to be found in the *Index Catalogue* (vol. v. 345, 354, 1884; vol. vi. 84, 1885; 2 s., vol. vi. 138, 159, 1045, 1901).

CHAPTER XXIX

Merosomatous Terata (*cont.*): Malformations of the Limbs: Sympodia (Definition, Frequency, Synonyms, History, Clinical Characters, Morbid Anatomy, Teratogenesis); Monopodia; Ectromelus or Amelus; Hemimelus; Phocomelus; Absence of Individual Bones; Miscellaneous Defects; Double Hand and Double Foot; Polydactyly and Hyperphalangy: Malformations of the Fœtal Annexa; Anomalies of the Placenta, Umbilical Cord, and Vessels.

THE malformations of the limbs form a long and varied series of anomalies. Few of them seriously affect postnatal life, but most of them require surgical treatment in order to remove the inconvenience they cause: they do not prevent the individual surviving his birth, but they greatly interfere with his usefulness, and they may, as in cases of amelia, so limit his activities as to make it impossible for him to earn his living save by exhibiting his deformity. I shall do with anomalies of the limbs as with those of other parts of the body; I shall describe one type in detail, and shall do little more than indicate the others. The type chosen for detailed description is sympodia or fusion of the lower limbs, for, in many ways, it has the greatest interest from the antenatal standpoint.

Sympodia.

Sympodia may be *defined* as a state of inversion of the lower limbs with a greater or less degree of fusion of the parts, and with an imperfect development of them and of the neighbouring pelvic organs and pelvis. This definition excludes the cases of rotation of the lower limbs without fusion, but it includes those of rotation with membranous adhesion such as my specimen (Fig. 35, p. 182); theoretically, also, it includes sympodia as it occurs in the allantoido-angiopagous twin (*vide* my article on paracephalus acardiacus, in which I describe a sireniform variety, *Trans. Edinb. Obstet. Soc.*, xviii. 210, 1892–93) and in united twins or double monsters, but I shall not specially consider these forms here.

Sympodia is relatively somewhat rare. It is true that a fairly long list of cases can be collected—I gathered together 116 instances up to 1897 (*Trans. Edinb. Obstet. Soc.*, xxiii. 74, 1898)—but then it must be remembered that it is a striking and arresting and clearly defined monstrosity, and that, therefore, it is most likely to be reported and preserved in museums or private collections. I have personally been able to examine three specimens (Nos. 121, 209, 250), and these are represented in Figs. 20, 35, 56, 63, and 83; since my list of cases of antenatal diseases and deformities numbers 331, sympodia may, therefore, be looked for about once in every hundred cases, and it is, therefore, not nearly so common as anencephaly (of which I had forty-six specimens). The proportion of cases of sympodia in general obstetric practice can hardly be even approximately stated.

Synonyms of sympodia are "cuspidate fœtus," "monopodia," "sirenomelia," "sirenia," "symelia," and "sireniform fœtus." The terms "mermaid fœtus" and "fœtus with a tailed appendage" have also been employed. None of these terms is quite so good as sympodia, which indicates the fusion of the lower limbs as the essential feature of the anomaly. Symelia, for instance, simply means fusion of limbs, upper or lower, and, as a matter of fact, fusion of the upper limbs is only known in cases of double terata (Fig. 90). To adopt the terms "sirenia" or "sireniform," and thus to liken the monstrosity to a fabulous creature (the siren), is scarcely scientific. "Cuspidate fœtus" is a fairly correct expression, indicating as it does that the fœtus "ends in a point," but it is somewhat pedantic. "Sympodia" is, therefore, the name I have chosen. "Monopodia," meaning one-legged, is quite inappropriate, for in cases of sympodia there is always evidence that two limbs have been more or less completely fused together to form the single lower extremity; there are, moreover, true cases of monopodia to which reference has already been made (p. 521).

The *history* of the early cases of sympodia is rather obscure. The earliest case seems to have been that of N. Rocheus (*De morbis mulierum curandis,* Paris, 1542): this I have not been able to see in the original, but Schenkius (*Observationum . . . . volumen,* lib. v. 737, 1609) described the same specimen as "monstrum superna parte hominis effigie ad umbilicum usque inferna syrenum caudam, pedum loco referens," and went on to state that Christian baptism had been given to it as it lived for at least an hour after birth ("tinctum fuit, hoc monstrum Christianorum lavacro, horamque a partu duntaxat vixit"). Another case was reported by J. Fincelius (*De miraculis sui temporis,* 1556–57). According to Taruffi (*op. cit.,* vii. 509, 1894), neither of these cases is referred to by C. Lycosthenes in his *Chronicon* (p. 142), published in 1557; he simply related a tale from Livy (Bk. xxxiv., par. 45) about an amelic fœtus; and, in Taruffi's opinion, he had an imperfect knowledge of sympodial fœtuses, since he confused them with examples of amelia and figured one with a penis and scrotum. I think, however, that Taruffi has, in part at least, misjudged Lycosthenes, for in my copy of his *Chronicon,* on page 623, is the picture of a fœtus sympus with arms and what looks like a vulva (which is evidently different from the specimen shown on page 142), and this instance is ascribed by Lycosthenes to Fincelius.

Aldrovandi (*Monstrorum historia,* 519, 1642) recorded a well-marked case, as may be gathered from the description he gave—"Ab umbilico autem, relicta hominis figura, in formam pyramidalem terminabatur, referens in cuspide similitudinem caudæ suis inflexæ." J. Scultetus (*Armamentarium chirurgicum,* p. 172, 1656) reported a dead-born fœtus which had neither anus, nor urethra, nor external genitals, but showed a perineal hernial protrusion and had the lower limbs closely united; the other parts of the body were well formed. Towards the close of the seventeenth century P. J. Hartmann (*Miscel. Acad. nat. curios.*, Dec. ii., Ann. x., obs. 162, p. 258, 1692) described his specimen, and was the first to give an account of the dissectional appearances; and Du Cauroi (*Journ. des. sçavans*, xxiv. (for 1696, p. 81) was told by a midwife about an infant, normal in its upper parts, which was without any appearance of distinction of sex and had a leg arising from the middle of the hypogastrium. Mery's "enfant monstrueux" (*Hist. Acad. roy. d. sc.*, Ann. 1700, 2nd edit., Paris, 1719, p. 42), although placed by Taruffi among the sympodial fœtuses, was really a case of inversion without fusion of the lower extremities.

In the eighteenth century nine new examples of sympodia were put on record, including two British instances, those of Superville (*Philos. Trans.*, xli. 302, 1744) and of Baster (*ibid.*, xlvi. 479, 1752). Hottinger described a case in 1706 (*Miscel. Acad. nat. curios.*, Dec. iii., Ann. 9, 10, p. 413, 1706), and Sue (*Hist. Acad. roy. d. sc.*, lxiv. p. 42, for 1746, Paris, 1751) met with one in which there were two uteri and a double thumb; but the most important contributions of the century were the two which came from the pen of A. K. Boerhaave (*Hist. anat. infantis cujus pars corporis inferior monstrosa*, Petropoli, 1754; *Hist. altera anat. infantis*, Petropoli, 1757). There were more than one hundred pages of description accompanying each of Boerhaave's records, and there were in all twenty-four plates illustrating very fully their anatomical peculiarities; even at the present time the observations of the St. Petersburg professor are well worthy of perusal. In this century also the long series of inaugural dissertations dealing with the subject of sympodia was begun with that of F. I. A. Rossi (*Diss. inaug.*, Jenæ, 1800).

The contributions of the nineteenth century were very numerous, and their bibliography up to the year 1897 will be found in my article already referred to (*Trans. Edinb. Obstet. Soc.*, xxiii. 74, 1898); but I may perhaps name those of Cruveilhier, Saint-Hilaire, Bardinet, Otto, Vrolik, Wolff, Julliard, Gebhard, Labougle et Régnier, Benington, Ruge, and Larcher as of special value. Since 1897 there have been several articles of merit, including those of Opitz (*Ztschr. f. Geburtsh. u. Gynäk.*, xl. 319, 1899), A. Guzzoni degli Ancarani (*Ann. di ostet.*, xxi. 609, 1899), L. Bolk (*Geneesk. Bl.*, vi. 301, 1899), E. Rabaud (*Bull. Soc. philomat. de Paris*, 9 s., v. 25, 1902–03), W. R. Stokes and R. L. M'Neer (*Maryland Med. Journ.*, xlv. p. 1, 1902), Audebert (*Toulouse méd.*, 2 s., v. 129, 1903), Abramoff and Riezanoff (*Arch. f. path. Anat.*, clxxi. 284, 1903), M. N. Poroskin (*Journ. akush. i jensk. boliez.*, xviii. 89, 1904), and Cichorius (*Arch. f. Gynaek.*, lxxii. 571, 1904). My three cases were published in 1898 (*Scott. Med. and Surg. Journ.*, ii. 296, 385, 1898), 1899 (*Trans. Edinb. Obstet. Soc.*, xxiv. 18, 1899), and in 1900 (*ibid.*, xxv. 144, 1900). A representation of the posterior appearances of the lower part of my first specimen is given in Fig. 83, while Figs. 20, 35, 56, and 63 give other views of it and of the two other cases.

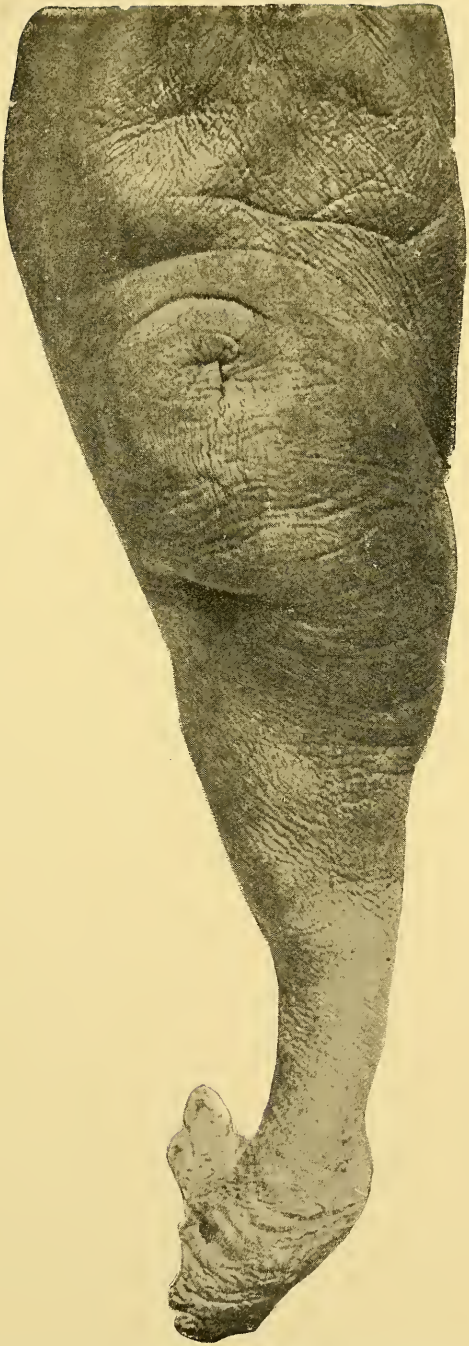

FIG. 83.—Posterior Aspect of Lower Part of a Fœtus Sympus Dipus, showing fused lower limbs and sinus over sacrum. Specimen No. 121.

The *clinical history*, antenatal and postnatal, of sympodial fœtuses requires no lengthy consideration. None of the recorded infants survived its birth for more than a few minutes, or at most, hours; but it is not quite clear to what cause this non-viability is to be attributed. The kidneys are frequently absent, and this may, perhaps, explain the early death of such monstrosities. No certain facts are forthcoming regarding the antenatal symptomatology of sympodia. In many cases a maternal impression (sight of a one-legged man, etc.) was referred to, generally after the event; in one case, curiously enough, the father had only one lower limb, the other having been amputated, but his other children were normal (Saint-Hilaire, *Histoire des anomalies*, ii. 246, 1836). The pregnancy seems somewhat frequently to have terminated prematurely, and reference has been occasionally made to the weakness of the fœtal movements or to the occurrence of an abdominal traumatism. In Ehrmann's case (*Musée d'anatomie . . . . de Strasbourg*, 1852) the father committed suicide during his wife's pregnancy which ended in the birth of a sympodial fœtus. In Gerrard's record (*Month. Journ. Med.*, xx. 348, 1855) there was hydramnios. All these occurrences, however, are quite exceptional, and the pregnancy was often absolutely uneventful. The labours, also, were often easy, delay, when it did occur, being commonly due to an associated malformation (*e.g.* hydrocephalus, as in my case) or to a malpresentation. When the fused lower limb presented, as it sometimes did, the diagnosis of the presentation was thrown into doubt.

Owing to the nature of the malformation the sex of the infant was often in doubt; but it was ascertained in a number of cases, with the result that neither sex could be said to preponderate.

The *morbid anatomy* of sympodia is a somewhat complicated subject. I shall consider, first, the external appearances, and, second, the conditions discovered by dissection.

The fused lower limb usually is directly continuous with the lower (sub-umbilical) part of the trunk, and it is commonly flattened anteriorly (Fig. 20) and curved posteriorly (Fig. 83). It is generally capable of being folded upwards upon the anterior surface of the trunk, so that, in one of my specimens, the fused foot lay over the right shoulder and near the right ear. In exceptional cases the lower limb arises at an angle from the trunk; sometimes, also, one segment of it moves freely upon the other, but, as a rule, the movement is chiefly at the hip joint. The lower part of the abdomen shows a tendency to narrow as it approaches the lower limb, and this tendency along with the form of the fused limb gives to the fœtus its cuspidate appearance. On the anterior aspect of the trunk near its junction with the lower limb there may be an indication of a penis (Fig. 20) or, rarely, of a vulva; generally there is no trace of external genitals. Posteriorly there is no indication of gluteal folds or anus; or a linear depression with radiating furrows may be visible (Fig. 83), which possibly indicates a rudimentary anal aperture. Not uncommonly a small tailed appendage is found situated posteriorly in the lumbosacral region; this caudal projection is due to a backward tilting of the lower end of the sacrum (Fig. 56); and the "tail" thus produced is not to be confused with the caudiform fused lower limbs.

The external appearances of the lower limb vary considerably, and the differences have been used as a means of classification. There are three varieties: according to the system of Saint-Hilaire (*Histoire des anomalies*, ii. 239, 1836) these are the genera, *symelus*, *uromelus*, and *sirenomelus*; according to that of A. Förster (*Missbildungen des Menschen*, 66, 1865) they are the types known as *sympus dipus*, *sympus monopus*, and *sympus apus*. In sympus dipus there are obvious signs that the single lower extremity is made up of two lower limbs: the digits number from 6 up to 10 or even 11, the foot is divided more or less deeply into two halves by a groove or fissure; three or four bones (2 tibiæ and 2 fibulæ, or 2 tibiæ and 1 fused fibula) can be felt in the leg; and 2 femora, more or less united, can be palpated in the thigh. The whole lower limb is inverted, so that the patellæ are situated posteriorly while the sole of the foot looks forwards (Fig. 20) and the dorsum backwards (Fig. 83). In sympus monopus there is more intimate union of the two conjoined lower limbs: the thigh and leg are narrower than in s. dipus; the two femora are fused into one; the leg contains only one or at most two bones; there is one patella situated posteriorly; there are rarely 5 digits, more commonly 2 or 1 (Figs. 56, 63). In sympus apus, the fused lower limbs end simply in a tapering point or in a stump like that seen after an amputation; there is here an even greater degree of fusion of the extremities, and a very defective state of the pelvis and its organs; no recognisable digit or digits exist. To these three distinct types Taruffi proposes to add a fourth: sometimes the lower limbs are rotated and united simply by membrane, as in one of my cases (Fig. 35); for this the name *epi-sympus dipus* has been proposed; the case of J. Labougle and P. C. Régnier (*Journ. de méd. de Bordeaux*, xviii. 438, 1889) ought probably to be placed in this group.

The body of the sympodial fœtus above the umbilicus is usually normal in its external characters. There may be associated malformations such as hydrocephalus, hare-lip, polydactyly, which alter the appearances of the head and limbs; sympodia itself, however, consists essentially in the sub-umbilical anomalies that have been noted.

The dissectional appearances are very interesting, and have been described in great detail by several authors, among whom I may name Boerhaave writing so long ago as 1754. The sacral and coccygeal vertebræ may be defective or excessive in number; and the tip of the spinal column may be directed backwards, or to one side, or even upwards, a circumstance which accounts for the occasional presence of a caudiform projection in the sacral region. The whole pelvis indeed is usually malformed. The ilia, in cases of absence of the sacrum, are united to each other and to the last lumbar vertebra by ligaments; these bones are also spread out laterally, so that the anterior superior spines are directed to the sides and downwards; their fossæ are flattened or even converted into convex surfaces. The tuberosities of the ischia are generally turned inwards, and their ascending rami are joined together in a horizontal plane with disappearance of the obturator foramina. In front of the ischia there is a projecting crest formed by the horizontal rami of the pubic bones. Sometimes the ischial and pubic bones unite to form a mass which may almost block the outlet of the pelvis, and may show a wide cotyloid cavity for the reception of the large head of the fused femora. These are the more usual anomalies found in the pelvis; less common malformations are the existence of a figure of 8 pelvic outlet and of membranous union of the symphysis pubis with outward displacement of the pubic bones. It is on account of these conditions that Taruffi (*op. cit.*, vii. 508, 1894) places sympodia among the pelvic monstrosities ("lecano-terata").

It is unnecessary to describe in detail the appearances revealed by a careful dissection of the lower limb. All degrees between complete fusion of the constituent bones, muscles, vessels, and nerves, and a simple membranous union of two outwardly rotated limbs may be met with. Where two acetabular cavities exist the femora have separate heads and shafts, and their great trochanters are situated internally, and are separate or united in part or completely. The femora are concave anteriorly and convex posteriorly, and they articulate usually with two tibiæ which are placed posteriorly or less commonly at the sides. In other cases the thigh bones are more or less fused, and have a single large head fitting into a single acetabular cavity; four condyles may be found inferiorly or three (two lateral and one large median one which represents the two external ones fused together); again, the shafts of the femora may separate inferiorly, showing two lower extremities, each articulating with a tibia. The femora in all these cases show rotation, external parts becoming internal and anterior parts posterior. The tibiæ also exhibit rotation, and so the "knee" flexes anteriorly. There may be two fibulæ situated internal to the tibiæ; or, more often, there is a single large fibula in the middle line of the leg. When there are only two femoral condyles there is generally a single tibia and no fibulæ. Nearly all the bones of both feet may be present, but, far oftener, the foot is represented by only two or three tarsal and metatarsal bones and the phalanges of one digit. When both feet are indicated, the heels are internal and anterior and the digits lateral or posterior.

Many of the internal organs are malformed in cases of sympodia. Those which are most affected are the genital and urinary organs. The kidneys, ureters, and bladder are generally absent, although the suprarenal capsules may be present. In forty out of fifty-two cases in which there was any reference to the state of the bladder it was declared to be wanting; and in the remaining twelve it was generally rudimentary, having no orifices. The urachus, although seldom referred to in descriptions of sympodia, was generally stated to be absent when any allusion was made to it (*Trans. Edinb. Obstet. Soc.*, xxiii. 64, 1898). The genital organs are usually very defective. A uterus has sometimes been found, but commonly only rudimentary ovaries and tubes or testicles without vasa deferentia are to be detected. There may be a cloaca opening posteriorly or not at all; in other cases the descending colon ends blindly. The diaphragm may show a defect causing hernia; the liver may be malformed; and the gall bladder may be absent, and so may the ductus venosus.

The state of the abdominal and pelvic blood vessels was fully investigated by me in my research already referred to (*Trans. Edinb. Obstet. Soc.*, xxiii. 54, 1898). In it I showed that in most cases of sympodia only one artery existed in the umbilical cord; in one instance (F. T. Majer, *Diss. inaug.*, Tubingæ, 1827) there were four vessels, regarded as an umbilical vein, an umbilical artery, and two omphalo-mesenteric vessels. In no case were there the three usual funic vessels. Further, out of thirty-five cases in which details of the abdominal vessels were given, there were twenty-five in which the single artery of the cord arose directly from the descending aorta, and passed towards the anterior abdominal wall in the middle line, carrying the peritoneum with it, and then turned upwards to the umbilicus. In most cases the absence of the hypogastric arteries was noted. Putting all these facts together I came to the conclusion that, in sympodia, the derivatives of the allantois (urachus and part of bladder) and its vessels (umbilical arteries and vein) were usually absent, and that the vessels of the cord were omphalo-mesenteric or vitelline in origin. The further conclusion seemed to me warranted, that in such cases the vascularisation of the placenta must be by the vitelline vessels.

The *teratogenesis* of sympodia is a subject which has been fruitful in ingenious explanations, and yet cannot be regarded as in any degree settled. Indeed, it is far from being settled. I have not, for instance, met with any explanation which explains the extraordinary rarity, the almost complete absence, of any cases of sympodia in the lower animals. Probably this is to be explained by differences in ontogenesis, and possibly by peculiarities in the comparative embryology of the allantois and placenta, but there is as yet little light upon the subject.

The two leading characters of sympodia for which an explanation has to be found are the fusion of the lower limbs and their rotation from within outwards and from before backwards; but the state of the pelvis, the absence of the bladder, and the presence of one artery in the umbilical cord also call for investigation. No theory yet advanced satisfactorily accounts for them all. Of course a mechanical compressing force suggests itself: it must drive the lower limbs together and at the same time rotate them outwards, and it is difficult to find in the muscles of the extremities, or in the uterine walls, or in the surrounding amniotic membrane such a peculiarly acting force. Further, it must be so exact in its action that only like parts (bone, muscle, vessel, and nerve) shall unite with like. Some light is thrown upon the problem by the study of the state of the lower limbs and caudal end of the embryo in early antenatal life. If the reader will look at Figs. 10 to 14 in this volume, it will become perceptibly less difficult for him to understand how the anatomical peculiarities may be produced; and if he further keep in mind that we have as yet no complete knowledge of the *normal* ontogenesis of these parts of the embryo, it will become apparent to him that with the acquisition of such knowledge some facts at present inexplicable might become easily explicable. I refer especially to the mode of the formation of the bladder, to the way in which the lower limb buds evolve and rotate, to the relation of the allantois and umbilical vesicle to the development of the placenta, and to the meaning of a single artery in the umbilical cord. Although I do not feel inclined to accept any one theory as a satisfactory explanation, I am yet constrained to think that Dareste's idea of an interrupted or arrested evolution of the caudal fold of the amnion and consequent pressure upon the underlying parts of the embryo produced thereby is essentially correct. At the same time it seems to be a possible hypothesis to affirm that the lower limb-buds may in a case of sympodia never actually exist separate, but are there from the very first as a single limb-bud or process. In other words, it is to my mind quite thinkable that the fused lower limbs of sympodia develop fused, possibly because the parts that normally lie between do not develop at all. It is unnecessary here, however, to open up this subject further; readers who are interested in these most difficult problems of teratogenesis will do well to re-read Chapters X., XI., and XII. with the special case of sympodia in view, and to consult some of the more recent monographs on the subject, such as those of Dareste (*op. cit.*, 2nd edit. p. 419, 1891), L. Bolk (*op. cit.*), and Rabaud (*Bull. Soc. philomat. de Paris,* 9 s., v. 25–62, 1902–03; *Bull. scient. de la France et de la Belg.*, 6 s., vi. 436–460, 1903).

Monopodia.

The term *monopodia* has sometimes been used as synonymous with sympodia, but if it be employed at all it ought to be restricted to the cases in which there is a single lower extremity which shows no indication that it had been derived from the fusion of two limbs. Some cases of this kind occur in association with gastroschisis of the lower lateral part of the abdomen; to them I have referred in Chapter XXVII. (p. 521). There are, however, other instances in which there is no such imperfect condition of the abdominal walls. Taruffi (*op. cit.*, vii. 549, 1894) has placed these two groups (with and without lateral gastroschisis) together, and, having found that in both there was absence of one os innominatum, has called them instances of *mono-anileus apus*. The cases in which there was no gastroschisis were those reported by Ahlfeld (*Arch. f. Gynæk.*, xiv. 276, 1879), by I. B. Budenz (*Diss. inaug.*, Marburg, 1862), by A. F. Tassani (*Gazz. med. ital. lomb.*, 2 s., i. 274, 1848), by G. Sacchero (*Ann. univ. di med.*, lv. 95, 1830), by G. Sangalli and by V. Colomiatti (cited by Taruffi, *Storia della teratologia*, vii. 551, 552, 1894). In this teratological state the presence of a single artery in the umbilical cord would seem to be a constant character; the artery, also, which is present would appear to rise from the aorta, and may, therefore, be vitelline rather than allantoic in nature. Ideas regarding the teratogenesis of monopodia have given rise to theories resembling those referred to under sympodia.

Ectromelus or Amelus.

Under the names *ectromelus* and *amelus* are placed the cases in which one or more of the four limbs is absent or reduced to a rudimentary stump. Some teratologists would restrict the term *amelus* or *amelia* to the cases in which all the four limbs were absent, retaining *ectromelus* for those in which one, two, or three of the extremities were affected; but it is difficult to carry out the distinction. H. Meunier (*Nouv. iconogr. de la Salpêtr.*, x. 15, 1897) has an interesting article on amelus, in which he gives bibliographical references to a number of cases. He divides all the recorded instances of it into *perfect* and *imperfect* specimens: in the former, neither the pelvic nor the thoracic girdles show the slightest trace of limbs, while in the latter there are indications of one or more limbs, of the nature of stumps containing one or more bones and varying in size and shape. Sometimes the stump can be seen to represent the upper segment of the aborted limb; at other times it represents the lower segment (hand or foot).

Cases of perfect or complete amelus are comparatively rare (Meunier has collected ten from literature), while incomplete amelus is less rare, although still far from common. Good instances of the former type are those reported by G. Joachimsthal (*Die angeborenen Verbildungen der oberen Extremitäten*, p. 5, 1900) and S. Cholmogoroff (*Centrlbl. f. Gynäk.*, xii. 819, 1888). In 1898 I had the opportunity of examining Dr. Gemmill Thomson's case of incomplete amelus shown at a meeting of the Glasgow Obstetrical Society. This infant, as may be seen from Fig. 84, had practically no arms, while its lower limbs were markedly dwarfed. Dr. Lindsay afterwards published a dissection of it, for the child died when six months old (*Trans. Glasgow Obstet. and Gynæc. Soc.*, ii. 16, 1898–1901). The dissection revealed the presence of two fragments representing the upper limbs: there was a humerus about 1 inch long on the right side, which fitted by a *concave* head on to a *convex* glenoid facet; while on the left side the humeral rudiment measured 1¾ inch in length and had a normal joint. The lower extremities were also anomalous. There was no acetabulum on either side; the femur consisted of two small cartilaginous nodules (the great trochanter and the lower epiphysis) united by a fibrous band (the head and shaft); the fibula was absent; the tibia was strongly curved forward; the tarsus was made up of one large cartilage (astragalus—os calcis) and two small cubes of cartilage; and there were three metatarsals and phalanges in series with them. There were many anomalies in the muscular system, and these occurred not only in connection with the limbs but also at a distance from them; there were likewise vascular variations and the sciatic nerve divided high up.

I have met with two other instances of incomplete amelus; in both the subject was a kitten. In one the right forelimb was apparently entirely absent, but dissection revealed a round mass of cartilage in a small glenoid cavity (*Interstate Med. Journ.*, vii. 367, 1900); this specimen I received from my friend, Dr. J. K. Drysdale. Of the other case I was able to examine only the scapula and rudimentary forelimb bone which were sent to me in 1902 by Dr. W. J. Stevenson of London, Ontario; the defective limb had been attached to the side by skin and fascia.

Little is known of the antenatal symptomatology of amelus; but it is noteworthy that in Gemmill Thomson's case the mother felt no fœtal movements during her pregnancy, and a glance at Fig. 84 will explain the reason. The malformation is not incompatible with postnatal life; indeed many amelic infants have lived to advanced ages, and have earned a living by the exhibition of their malformation and by the marvellous way in which they have adapted a foot or a hand to do the work of all the limbs. In this relation I need only refer to Miss Biffin, to Mr. Buckinger, to Thomas Pinnington ("born without hands, feet, or legs—to be seen at the Goat at Charing Cross—he makes his own Pens, writes well, beats a Drum, plays at Cards—he stands upon the Crown of his Head on the Bottom of a Drinking-Glass"), to Thomas Roberts, to Antonio Morretti ("the astonishing Podothaumanist"), and to Thomas Schweicker. In recent years there have been the famous cases of John Chambert, of Unthan, and of Charles Tripp ("the armless man" of Barnum's Show).

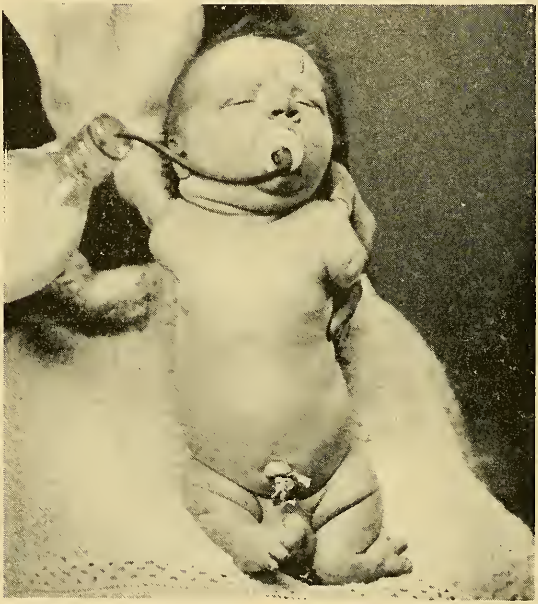

FIG. 84.—Case of Ectromelus or Thoracic Amelus.

Hemimelus.

Hemimelus is the name given to those cases in which one or more of the four extremities ends in a more or less tapering point or stump resembling that left after an amputation at the ankle, wrist, elbow, or knee; the proximal end of the limb is generally well developed and complete, while the distal is absent or greatly reduced. It includes nearly all the instances of so-called *spontaneous amputation* (*vide* Vol. I. of this MANUAL, p. 396; also pp. 150 and 186 of the present volume). A typical example was brought under my notice several years ago by Dr. T. B. Darling; it is represented in Fig. 37 (p. 137); and I have already (*vide* Chapters X. to XII.) dealt at some length with the whole subject of these malformations and their mode of production.

Hemimelus is a comparatively common defect, at any rate in its minor degrees, and it has a very large literature. Several hundred cases might without much difficulty be collected together, the only difficulty being that they are scattered and that indexes and lists have been in the habit of entering them under various headings. The *Index Catalogue*, for instance, gives some references under *Extremities* (*Abnormities and Deformities of*) in vol. iv. pp. 439, 440, 444, 1883, and in 2 s., vol. v. pp. 231, 236, 240, 1900; others are found under *Amputations* (*Intrauterine*), in vol. i. p. 244, 1880, and in 2 s., vol. i. pp. 318, 321, 1896; and others under *Monsters, from defect or malformation of limbs*, in vol. ix. p. 420, 1888.

Hemimelus may affect one or more limbs in the same patient, and while causing no disturbance in antenatal life may be the cause of much inconvenience after birth. The rounded or conical stump, which not infrequently carries several rudimentary digits, is of little value as a hand or foot, and has to be supplemented by various mechanical devices to ensure a certain degree of usefulness. In this deformity, as in amelus, the individual usually acquires great dexterity with the normal extremities (*e.g.* with the feet when the hands are deformed).

Since I have already considered at some length the teratogenesis both of amelus and hemimelus (Chapters X. to XII.), I need not return to the subject here; but I may refer to one or two recent cases which throw some light upon the subject. Gasne's case, for instance, was the child of a man who was in the active secondary stage of syphilis at the time of his conception (*Nouv. iconogr. de la Salpêtr.*, x. 31, 1897); in a case reported by E. Huet and C. Infroit (*ibid.*, xiv. 128, 1901) there was seen one of those intermediate types between hemimelus and phocomelus, which are so troublesome when we try to classify instances of deformity of the limbs; and E. Fournier (*Stigmates dystrophiques de l'hérédo-syphilis*, p. 158, 1898) recorded several examples of hemimelus in individuals the subjects of hereditary syphilis.

Phocomelus.

The phocomelous fœtus is one in which the proximal and not the distal segments of one or more limbs is aborted. It contrasts markedly on this account with hemimelus, in which the distal segment is the affected part. The result is that a foot or a hand seems to spring directly from the trunk, giving to the extremity or extremities the appearance of the flippers of the seal (*phoca*). This character is well displayed in Fig. 85, which represents the specimen of phoco-

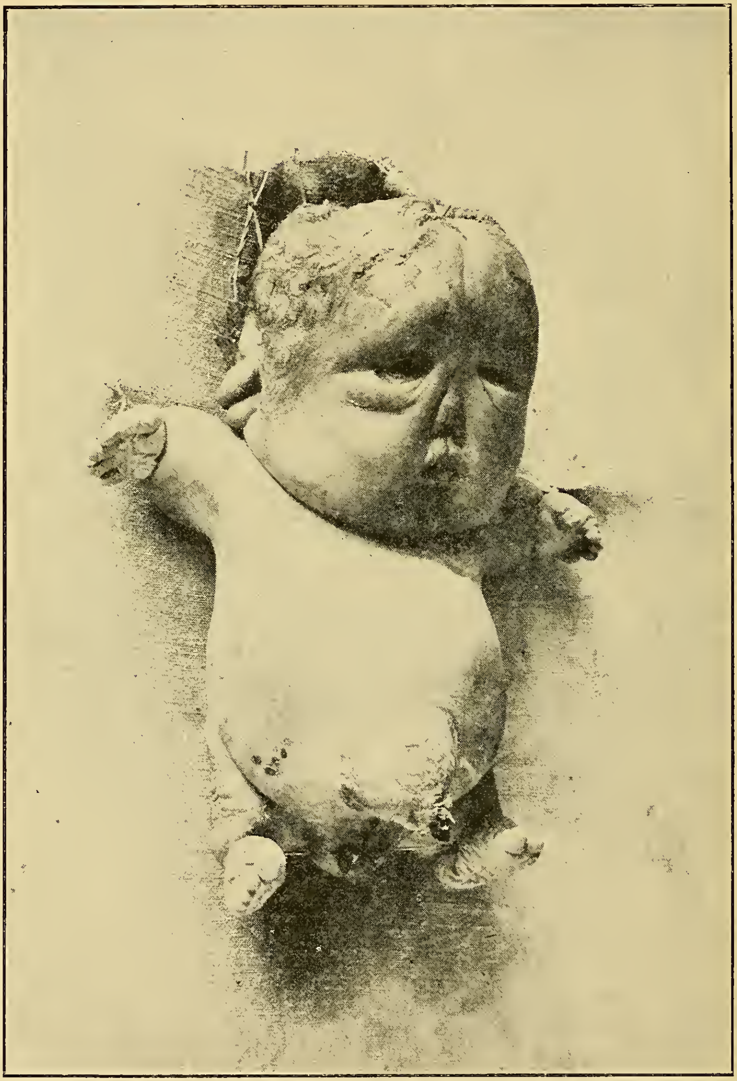

Fig. 85.—Specimen of Phocomelus, showing also an Umbilical Hernia.

melus, affecting all the four extremities, which was described by Baxter Tyrie and J. W. Haigh in my journal in 1894 (*Teratologia*, i. p. 89, 1894); I have also reported and figured a case of the same type of monstrosity in the first volume of this MANUAL (p. 351).

Possibly there is proof of the occurrence of phocomelus as far back in the world's history as the early times of Babylonian rule, for in the teratological records of Chaldea (*vide* my article in *Teratologia*, i. 133, 1894) there is the account of an infant whose hands and feet are like four fishes' tails or fins. Of course, this may have been nothing more than an instance of the more common malformation known as syndactyly or webbing of the digits. At any rate, many cases of phocomelus have been reported, and since the deformity does not interfere with postnatal life, and may be used for exhibition purposes, it is easily understood that some of them have gained notoriety. I need only refer to Marc Cazotte or Pépin, to the "turtle woman" of Demerara, and to Nicodemus, "the Nondescript Negro from Texas." An interesting case of pelvic phocomely was reported by J. Roubinovitch (*Compt. rend. Soc. de biol.*, 10 s., v. 819, 1898): the patient, a boy of thirteen years of age, was the child of a man who was an inveterate absinthe drinker; at birth a loop of the umbilical cord was noted surrounding the left lower limb; the morbid anatomy of the case showed that there were only three toes in one foot, and there was, therefore, some degree of hemimelus as well as phocomelus.

Although external examination would seem to show that many phocomelous fœtuses possess nothing more than the distal segment of one or more limbs, dissection generally reveals the presence of other parts than those of the hand or foot alone. Thus in Baxter Tyrie's case (*loc. cit.*) there was in the upper limb an aborted glenoid cavity to which a spindle-shaped bone (humerus) was attached by fibrous cartilage; the radius and ulna had no upper or lower epiphysial cartilages; there was no proper elbow joint; but the carpus and manus were normal. The lower limbs were slightly better developed, for they showed normal hip joints, each with a ligamentum teres; the femora, however, were stunted; and there was no knee joint, the tibia and fibula being simply united by fibrous tissue to the thigh bone of the same side. In my case of phocomelus, figured in Vol. I. (p. 351), the bones of the thigh, leg, upper arm, and forearm were indicated solely by tiny cartilaginous rudiments; and in one of Joachimsthal's cases (*op. cit.*, p. 10) skiagrams showed no bony connection between the skeleton of the hand and that of the shoulder girdle.

The phocomelous monstrosity may exist alone or it may be associated with other malformations. Thus, in Baxter Tyrie's specimen, there were various muscular anomalies—an umbilical hernia, an inguinal hernia on the left side, undescended testicles, a penis with complete absence of corpora cavernosa, a diaphragmatic hernia on the left side, a cleft palate, a perforation in the interventricular septum of the heart, and a spina bifida in the dorso-lumbar region. In my specimen there was defective ossification of the frontal bones.

Some confusion has been introduced into the study of cases of phocomelus by the employment of the term *micromelus* as a synonym. It is better to allow this word to signify any dwarfing of the limbs whatever, including the results of fœtal bone disease (achondroplasia), and to reserve the names amelus, hemimelus, and phocomelus for the varieties which have been described above. At the same time it is not possible, in my opinion, to separate exactly the deformities of the limbs due to fœtal diseases and the malformations due to arrested embryonic ontogenesis; there is a certain amount of overlapping (*vide* Vol. I. p. 352).

Absence of Individual Bones of the Limbs.

Cases of congenital *absence of the tibia* are occasionally met with. Sometimes the whole bone is absent; at other times it is only a part that is wanting, generally the lower end. The anomaly may be unilateral or bilateral. It is generally associated with other defects, such as absence of the patella, imperfect development of the lower end of the femur, thickening of the fibula, cutaneous scars (amniotic ?), club-foot, and digital malformations. Many valuable monographs on absence of the tibia have been published; I may refer specially to Ludwig von Muralt's article in the *Bibliotheca Medica* (Abth. C., Heft 5, 1896), to Mario Motta's (*Arch. di ortoped.*, xiv. 65, 152, 1897), and to J. S. McLaren's (*Journ. Anat. and Physiol.*, xxiii. 598, 1888–89).

Absence of the fibula is more frequently met with than absence of the tibia. P. Mazzitelli (*Arch. di ortoped.*, xv. 310, 1898) gathered together and analysed 120 cases, finding that the defect was bilateral in 37·7 per cent. and unilateral in 62·3 per cent., and that it was complete in 69·7 per cent., partial in 24·7 per cent., and mixed (partial on one side, complete on the other) in 3·6 per cent. Apparently the male sex is more liable to this malformation than the female (as 69 to 23). The leg is shortened, shows a marked curve with convexity anterior and with a depressed scar over it, and has a foot in the position of valgus or equino-valgus. Other malformations may occur in association, such as absence of one or more toes, of the foot, of the femur, or of the tibia. Fracture of the tibia may also occur as a complication. Recent articles on this subject are those of H. Rheinheimer (*Diss. inaug.*, Würzburg, 1898), of Cotton and Chute (*Trans. Amer. Orthop. Assoc.*, xi. 316, 1898), of H. L. Taylor (*Pediatrics*, viii. 297, 1899), and of R. Froelich (*Gaz. hebd. de méd.*, n.s., v. 49, 1900). A good account was given by E. Kirmisson in his *Traité des maladies chirurgicales d'origine congénitale* (p. 551) in 1898.

Complete or partial *absence of the femur* is very uncommon as an isolated deformity. H. Grisson, however, reported a case in which only the upper and lower ends of the left femur existed; the leg and foot were normal in length and structure (*Arch. f. klin. Chir.*, xlix. 252, 1894). R. A. Cleeman (*Pediatrics*, vi. 499, 1899) has met with congenital absence of both femurs; a similar observation was put on record by W. R. Williams (*Trans. Path. Soc. Lond.*, xxxv. 317, 1883–84). Other cases were those of F. Lange (*Deutsche Ztschr. f. Chir.*, xliii. 528, 1896), of G. Lotheissen (*Beitr. z. klin. Chir.*, xxiii. 139, 1899), and J. H. Morgan (*Trans. Chir. Soc. Lond.*, xvi. 259, 1882–83).

Absence of the patella on one or both sides is another malformation of the leg bones which has of recent years been shown to be less rare than was supposed. Lane (*Lancet*, i. for 1858, p. 63) noted an instance of it affecting the right side in 1858; Labbé (*Bull. Soc. de chir. de Paris*, 3 s., iii. 508, 1874) saw a bilateral example of it; and W. Körte reported two cases (*Deutsche Ztschr. f. Chir.*, vii. 69, 1876). More recent records are those of Bousquet (*Bull. et mém. Soc. de chir. de Paris*, n.s., xi. 354, 1885), of M. Salaghi (*Arch. di ortoped.*, xi. 222, 1894), and of G. Phocas and G. Potel (*Rev. d'orthop.*, vii. 342, 1896). In individuals suffering from this defect it is easy to feel the condyles of the femur, the groove between them and the anterior tuberosity of the tibia; there is also a transverse fold of skin on the front of the knee joint during extension; and there is sometimes dislocation forwards of the head of the tibia. The deformity known as *genu recurvatum* is associated with an apparent or a real absence of the patella. I met with a case of bilateral genu recurvatum in July 1899. It was that of a female infant, ten days old. The cranial ossification was good and the muscles were everywhere well developed, but there was considerable lumbar cyphosis with compensatory lordosis higher up; and the femora and humeri appeared relatively short. There was hyperextension of both knees; instead of the normal flexion at the knee, each leg formed with the thigh an angle open to the front. There was, therefore, no popliteal space in the sense of a depression; but in the position thereof was a projection recognised to be that caused by the femoral condyles protruding backwards behind the heads of the tibia and fibula. In front were several folds of skin due to the relaxation of the tissues caused by the forward flexion. The upper end of the tibia and fibula lay dislocated forwards in front of the lower end of the femur; and no patella could be felt, nor did the Röntgen rays reveal one. The forward flexion of the knees, which was accompanied by a certain amount of external lateral displacement, could be increased by manipulation; but the limbs could not be entirely straightened without anæsthesia. The infant was the result of the first full-time pregnancy of a mother who had on a previous occasion had an abortion followed by pelvic abscess. The labour was long and the liquor amnii was scanty. The parents were first cousins, and their marriage was not the only one between blood relations in their family. In this case there was some improvement under treatment; and Bilhaut (*Ann. de chir. et d'orthopéd.*, x. 257, 1897) in a similar case obtained a satisfactory result after ten years. Many important articles have appeared on the subject of genu recurvatum and its treatment during recent years (*vide* the *Index Catalogue*, 2 s., viii. 762, 770, 1903).

Absence of the radius occurs more commonly than that of the ulna, and it is nearly always associated with *club-hand*. I have met with three cases in which these malformations occurred together. The first was a stillborn premature male infant given to me for examination by Dr. T. B. Darling in 1890. Both the feet and the hands were clubbed, and there was absence of the radii; the thumb was also wanting on the left side; and there was non-descent of the testicles and imperforate anus. This was specimen No. 21 in my list. The other two cases were the offspring of healthy parents, but the mother had defective formation of the short muscles of both thumbs. She had two normal male infants, next she aborted, and then she gave birth to a hydrocephalic female fœtus with absence of the right thumb and radius and club-hand on that side (Fig. 62, p. 360). In subsequent pregnancies she had two normal infants, an anencephalic female infant, and finally a premature female infant with absence of both radii and the right thumb and with commencing hydrocephalus. I described and figured these fœtuses in an article published in 1900 (*Amer. Journ. Obstct.*, xli. 577, 1900).

W. Kümmel (*Bibliotheca Medica*, Abth. E., Heft 3, 1896) has collected together the literature of this malformation and has also described four new cases; Kirmisson also gave a good account of the deformity in his *Maladies Chirurgicales* (p. 460, 1898). The radius may be partly or entirely absent, and the latter state is the more common; both sides of the body may be affected, but the unilateral variety is a little more common, although neither one side nor the other predominates. The hand is turned to the radial side of the arm, the thumb with its metacarpal bone and some of the outer bones of the carpus are absent, and various muscles of the arm and hand are wanting. When the radius is only partly absent, it is usually the lower end that is defective; but a few cases have been reported in which the upper end was affected, and in them there was no club-hand. It is necessary, of course, to remember that club-hand does not always accompany radial defects, and also that it may occur apart from these deformities (*e.g.* in absence of the ulna) and even in individuals otherwise well formed. When there are some associated malformations they do not necessarily affect the limb or limbs in which the radius is absent, but may occur in distant parts (*e.g.* atresia of the anus, defect of the ear, hare-lip, cleft palate, and horse-shoe kidney). I have a skiagram of a case of absence of radius which I got from Professor Jardine in 1897; there was a small meningocele in the occipital region as well as absence of the thumb.

Absence of the ulna is less common: Kümmel (*loc. cit.*) was able to collect only thirteen cases from literature, while he had gathered sixty-seven instances of defect of the radius. Among Kümmel's thirteen cases was that reported by J. H. Pringle (*Journ. Anat. and Physiol.*, xxvii. 239, 1892–93) in which the deformity was bilateral. There commonly is deviation of the hand to the ulnar side, and movement at the elbow joint is interfered with. In the case of a man whom I examined in Professor Chiene's Ward in the Edinburgh Royal Infirmary in October 1902, the head of the right radius was enlarged and displaced upwards and outwards; the internal condyle of the humerus was also large; the head of the ulna was defective; and the fourth and fifth digits of the right hand were absent, while the little finger of the left hand was double. Symmetrical ulnar defect is not common, and associated malformations are not so often met with as in cases of absence of the radius. In Gessner's case, however, in which the right ulna and corresponding fingers were absent, there was a diaphragmatic hernia and a uterus unicornis (*Centrlbl. f. Gynäk.*, xviii. 824, 1894); while in R. G. Collins' patient there was absence of one fibula, an imperforate anus, club-foot, and a defective penis (*Chicago Clin. Rev.*, iv. 11, 1894–95).

Absence of the humerus, as an isolated defect, would appear to be very rare. J. C. Gittings (*Arch. Pediat.*, xv. 927, 1898), indeed, reported a case in which there was apparently no humerus, but there was a very rudimentary radius and ulna and a defective carpus, so that it seemed that it might rather be classed as an instance of phocomelus than of absence of the humerus.

Miscellaneous Defects of the Limbs.

I have only space to name the many minor malformations of the extremities which may be met with. Some of them, such as club-foot in its different varieties, may be regarded as the result of pressure during the later months of antenatal life or as due to fœtal diseases; but others, such as absence of digits, must be referred to the embryonic period of existence.

Club-foot is so fully considered in so many easily accessible text-books that I need do no more than mention it, pointing out that it differs essentially from club-hand; for the latter is more than a displacement of parts, being due to actual defects and associated anomalies (*e.g.* absence of radius or ulna), while the former is merely a distortion, and is accompanied by other anomalies only in comparatively rare cases.

Ectrodactyly is the term applied to defects of the digits, such as complete or incomplete absence of one or more fingers or toes. In some cases all the digits of one limb may be wanting (total ectrodactyly), in others we find one or more digits in a normal state (partial ectrodactyly). Sometimes the fingers or toes that are present are shorter than normal (*brachydactyly*), and the shortness may be due either to absence of one segment or to diminished size of all the segments; very often the digits that are left are joined together by webs of skin (*syndactyly*). Both brachydactyly and syndactyly may also exist apart from ectrodactyly. Amniotic bands have not infrequently been noted in connection with ectrodactyly (Fig. 36), as I have pointed out already in discussing the causation of malformations (p. 184). An interesting variety of this deformity is called *bidactyly* or the "lobster claw" anomaly: in it two digits alone are left, usually the thumb (or great toe) and the little finger or toe, and thus the appearance of the two claws is produced. I have in my possession a good skiagram of this malformation which was given me by the late Dr. George Elder in 1899; the patient was a man whose left hand carried a thumb and a little finger with two phalanges, all the intermediate digits being absent. A recent case in which all the extremities were affected was that of Le Roy des Barres and Gaide (*Gaz. d. hôp.*, lxxvii. 697, 1904).

Sometimes there is a fissure dividing a hand or a foot into two nearly equal parts; this constitutes the deformity called "split-hand" (*Spalthand*) and "split-foot" (*Spaltfuss*) by Kümmel (*loc. cit.*, p. 47). The middle finger with its metacarpal bone or the middle toe with its metatarsal is absent in this deformity; sometimes the remaining pairs of digits are united by skin folds (syndactyly). All the extremities may exhibit this anomaly. It may also be transmitted hereditarily as in the curious case related by Kümmel (*loc. cit.*, p. 21): the history given was that the great-grandfather (on the father's side) of the little patient with the split-hand had wounded the middle finger of his left hand to save himself from military service; his son had no fourth finger on the left hand; four of his children had defects of fingers; and the patient (his great-granddaughter) had no fourth finger or metacarpal bone on her left hand. This is an example of hereditary transmission, but it is doubtful if it can be alleged as an instance of an acquired defect becoming hereditary.

Absence of thumb (radial ectrodactyly) and its metacarpal is usually associated with absence of the radius, as has been stated already; but it may also occur as an isolated defect, as in P. Ehrhardt's case (*Rev. d'orthop.*, i. 205, 1890). Lateral deviation of the thumb, constituting a sort of club-thumb, has been observed by G. Joachimsthal (*Ztschr. f. orthop. Chir.*, ii. 441, 1892–93); Kümmel (*loc. cit.*, p. 19) saw a similar defect in a patient in whom the upper part of the radius was absent.

Dislocations of the hip, knee, shoulder, and elbow may be met with at birth, and have been referred to already (Vol. I. p. 49). Their causation is obscure, but some of them at least are probably embryonic in origin, if we may judge from the malformations of the joints and the occurrence of associated anomalies which are undoubtedly teratological. An enormous literature has of late years grown up round congenital dislocation of the hip, more especially in connection with operative interference.

Double Hand and Double Foot.

Under the names *dichirus* and *dipus* have been described a few cases of apparent duplication of the terminal segment of a limb. Such deformities ought strictly to be discussed among the polysomatous or double terata, but since they lie on the border line between the two great groups of monstrosities I may refer very briefly to them here.

In November 1892 I showed to the Edinburgh Obstetrical Society a male infant with a bifid hand (*Trans. Edinb. Obstet. Soc.*, xviii. 1, 256, 1893). It was the right hand that was affected, and its appearances are shown in Fig. 86. The hand hangs down in a helpless fashion, reminding one of the "wrist-drop" in lead-poisoning, and the arm tends to be pronated and half-flexed at the elbow joint. There are seven digits, divided into two groups, a radial and an ulnar, by an interdigital sulcus: the ulnar group consists of four digits, each made up of three phalanges, and these represent the little, ring, middle, and index fingers; the radial group consists of three digits, probably the little, ring, and middle, each having three phalanges. The elbow joint was abnormal; there was pain and creaking on manipulation, and it seemed as if the ulna were dislocated inwards. The deformity is to be looked upon as a case of fusion of two hands with absence of the thumbs; it is as if the right and left hands were welded together, the index of the one coming into juxtaposition with the middle finger of the other.

Shortly after I published this case I received a letter from Professor Dwight drawing my attention to his article on "Fusion of Hands" (*Mem. Bost. Soc. Nat. Hist.*, iv., No. 10, 1892). In this article a case was described very similar to mine but with a dissection of the parts after death. In it there was no radius in the forearm but two bones which Dwight regarded as two ulnæ, each with an olecranon process; the lower end of the humerus was also double, consisting of an internal condyle on each side and two fused external condyles in the middle line. On re-examining my case I came to the conclusion that a similar state of the bones of the forearm existed in it.

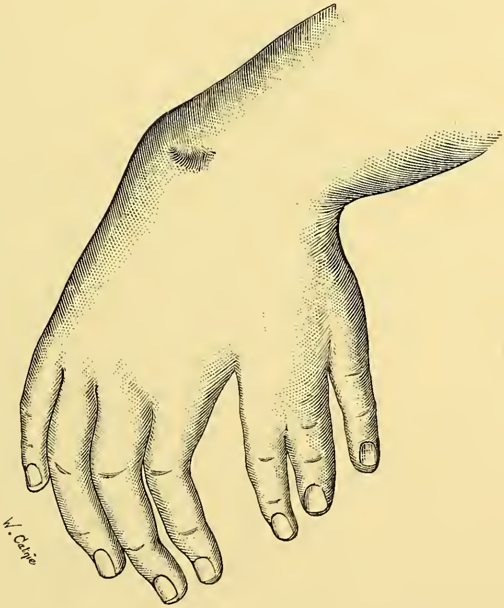

Fig. 86.—Case of Double Hand (*Dichirus*).

In addition to Dwight's example of double hand there have been a few others, among which I may mention J. Jardine Murray's (*Med.-Chir. Trans.*, xlvi. 29, 1863), C. Fumagalli's (*Ann. univ. di med.*, ccxvi. 313, 1871), F. Jolly's (*Internat. Beitr. z. wissensch. Med. . . . Festschr. R. Virchow*, i. 617, 1891), and that of M. Giraldès (*Maladies chirur-*

gicales des enfants, p. 42, 1863). Double foot (*dipus*) is also met with, but rarely apart from sympodia; a probable instance was that reported by B. E. Brodhurst (*Lectures on Orthopedic Surgery,* p. 55, 1876). I also saw a case in Professor Chiene's Ward in the Edinburgh Royal Infirmary in 1894 that was possibly of this nature. It was that of a little girl, four years of age, who had five fingers on each hand, the first digit in each having three phalanges. There were seven toes on each foot, the first and second being united by a fold of skin in both; the third toe in both had only two phalanges. The heel of the right foot was drawn up by the tendo Achilles, and there was also marked inversion; the left foot was less deformed than the right, but the left leg was much shorter than the right, and there was enormous thickening of the upper part of the fibula. It was a remarkable fact that the mother of this child had also seven toes on each foot, that two of her sisters had six toes and five fingers, and that the grandfather had the toe-nail of the hallux double. I am of opinion that this little girl showed a condition of fusion of two imperfect feet and that the so-called fibula may have been a second tibia.

Such malformations are very difficult of explanation, whether we regard them as instances of fusion of hands and feet or as polydactyly. The theory of atavism is inadequate; and it is almost impossible to accept the idea that the double hand or foot represents united twins which have lost all other signs of duplicity. These cases are even more inexplicable than double penis (diphallus) and double bladder.

Polydactyly.

In 1893 I contributed an article on six cases of polydactyly (*Arch. Pediat.*, x. 573, 1893). Three of the cases occurred in the same family, and they may be taken as typical of the common form of polydactyly. The mother and father had no digital deformities, but all their three children (a boy and two girls) exhibited sexdigitism. The boy had six toes on each foot: on the right side the supernumerary toe, with three phalanges, was attached to the outer side of the distal end of the fifth metatarsal, and closely resembled the fifth toe and lay parallel with it; on the left side the extra digit also had three phalanges, but it articulated with the proximal phalanx of the fifth toe instead of with its metatarsal bone and it projected outwards from the foot. In one of the girls (next in age to the boy) there were also six toes on each foot: her right foot clearly resembled her brother's left, the extra toe being attached to the outer side of the proximal phalanx of the fifth digit but without projecting outwards so markedly; her left foot, however, showed an accessory toe intercalated between the fourth and fifth and shorter than either; her left hand had a small nodule (rudimentary digit?) attached to the junction of the proximal phalanx of the little finger with the corresponding metacarpal bone. The third child (a girl) had a right foot resembling her brother's left and her sister's right, the extra digit being attached to the outer side of the proximal phalanx of the fifth toe; on the left foot there was also a supernumerary toe, consisting of two phalanges, fixed by a narrow pedicle to the outer side of the foot at the level of the proximal phalanx of the fifth toe.

These cases may be taken as characteristic instances of the commoner types of polydactyly. Rarer types are found in the instances of ten, nine, eight, and seven digits which have been from time to time reported and which are gathered together by Taruffi (*op. cit.*, iii. 425, 543, 1885; viii. 487, 1894) and other teratologists and pathologists. Various anomalies of the metacarpals, metatarsals, carpus, and tarsus may be associated with polydactyly, and the extra digits themselves may be webbed or shortened or otherwise defective. The hands are more often affected than the feet; and the supernumerary fingers and toes are generally attached to the ulnar and fibular sides of the limbs, less often to the radial and tibial, and rarely are they intercalated between the normal digits. Male infants are more often affected than female; and sometimes more than one limb in the same individual shows polydactyly.

Various degrees of bifidity of the thumb and great toe may be met with, from a simple division of the nail into two (as in a little boy whom I examined in 1892) to a complete doubling of the digit. A teratological state which may be mentioned here is the three-phalanged thumb; this condition of *hyperphalangy* or *triphalangy*, as it is called, presents one of the most puzzling problems which await solution by the antenatal pathologist. Four phalanges have been found in the index and middle digits; so that it is not possible to explain away the triphalanged thumb by calling it a duplicated index.

The *teratogenesis* of the anomalies of the limbs that are characterised by excessive formation or development is surrounded with great difficulty. The amniotic theory has to be forced beyond reason to include such malformations as polydactyly. Of course it may be held that an amniotic band or cord may so press upon a digit or upon the foot or hand in its undifferentiated state as to divide it into two or more parts; but it is difficult to fit the facts to such a view, for amniotic defects are very rarely associated with supernumerary digits, and the occurrence of syndactyly as a complication of polydactyly introduces another difficulty not easy of explanation.

One fact is widely known and must be taken into account. I refer to the hereditary nature of these malformations. Many instances, some historical in their importance, may be brought forward in proof of this assertion; and not through two generations but through many the deformity may be traced in certain cases. For this reason one is led to refer the cause of polydactyly back to the germinal period of antenatal life, and to look for an explanation in the phenomena of atavism. Here, also, there are manifest difficulties, and in the meantime it is perhaps best, or at least safest, to speak of a tendency to excessive formation existing in the germ, a sort of ill-regulated or uncontrolled gemmation of the distal extremities of the limbs, associated perhaps with anomalies in nutrition. The *literature* of the various malformations of the limbs is enormous. The reader will find many references in the *Index Catalogue* under such various headings as *Fingers and Toes* (vol. iv. 979, 1883; 2 s., v. 797, 1900), *Extremities* (vol. iv. 439, 440, 444, 1883; 2 s., v. 232, 236, 240, 1900), *Foot* (vol. v. 65, 1884; 2 s., v. 926, 1900), *Hand* (vol. v. 816, 1884; 2 s., vi. 725, 1901), *Monsters* (vol. ix. 420, 1888), etc.

Malformations of the Fœtal Annexa.

It is difficult to decide where to place the malformations of the fœtal annexa in a MANUAL OF ANTENATAL PATHOLOGY. Are they fœtal, embryonic, or germinal in origin? Some of them are undoubtedly fœtal and have been considered in the first volume of this work (p. 400). Others must be looked upon as germinal, for it must not be forgotten that some of the fœtal annexa, *e.g.* the amnion and the chorion, precede the embryo in the order of development; for this reason amniotic anomalies and chorionic degenerations may take their origin at a time in antenatal life anterior to the appearance of the embryonic rudiments in the embryonic area of the impregnated ovum. But there are yet others which may fairly be believed to be produced in the embryonic period; and among these may be named placental anomalies, persistence of the umbilical vesicle and its vessels, and malformations of the umbilical cord. It will be remembered that in dealing with teratogenesis I described at considerable length anomalies of the amnion (narrowness, adhesions, bands, etc.) and their effects or supposed effects upon the developing embryo, so that I need not consider them again either here or under the pathology of the germ. Malformations of the early chorion, such as hydatid mole, will be briefly referred to under germinal pathology. For these reasons I take up here only the anomalies of the placenta, umbilical cord, and umbilical vesicle; these form a sort of natural group, somewhat closely related to each other.

Placental malformations are probably less rare than is usually stated, for many cases pass unnoticed through want of careful examination. One of the less common types is that known as the *dimidiate* or *duplex* placenta. I received in August 1904 a specimen of this kind from Dr. Lewis Hughes of Dowlais, Glamorganshire. The placental mass consisted of two parts one of which was the size and shape of an ordinary placenta, the other was a little less in size, had an irregular shape, and was thinner than usual; the cord was inserted along the line of union of the two masses; and in the neighbourhood of the smaller part there were two smaller placental lobules (*succenturiate lobes*). There was only one infant, and Dr. Hughes had some difficulty in detaching the second and thinner part of the afterbirth during the third stage of labour. On the fœtal surface of the larger part a persistent umbilical vesicle could be recognised. I have seen another almost perfect specimen of placenta duplex, that shown to the Edinburgh Obstetrical Society by Dr. James Ritchie in 1895 (*Trans.*, xx. 88, 1895). In both these instances the single cord had an insertion into the membranes. Another specimen was shown by Dr. Graily Hewitt in 1866 (*Trans. Obstet. Soc., Lond.*, viii. 337, 1867); but in that instance the cord divided into two branches, which were inserted far from each other into the two placental masses, near their margins.

Much more common than the dimidiate placenta is the presence of one or more small lobules of placental substance attached to the membranes near the chief mass; these extra lobules are called *succenturiate.* They are supplied with small branches of the umbilical vessels which pass to them from the placenta in the membranes. Their clinical significance is the risk of their being left in the uterus after the third stage of labour; their pathological or teratological significance is not obvious.

In some cases the placenta has the form of a *horse-shoe* or of a *kidney* instead of being discoidal, there being a defect at one part or another causing a sulcus between the two large segments of the organ. Rarely the placenta has had areas in it showing simply the chorion with no placental substance, and yet the outline has been regular; to this variety the name *placenta fenestrata* has been given. Another anomaly is called the *placenta membranacea*; in this the organ is widely diffused and thinned out, and it may occupy as much as four-fifths of the whole area of the chorion. I have met with one or two instances of this, but of less extent than that indicated above. The anomaly is apt to lead to hæmorrhage in the third stage of labour. Another anomaly is that in which the whole placental tissue is localised to a comparatively small area of the surface of the chorion; the placenta then takes a peculiar conical form (*placenta conica*).

One of the most interesting of the placental anomalies is that in which a strip or margin of the organ all round the circumference projects beyond the line of attachment of the membranous sac; to this arrangement the name *placenta marginata* or *circumvallata* is given. In a case of this kind which I saw in 1899 the space within the membranes near the placenta was much diminished; the child, a male, was small for the age of pregnancy arrived at (eight and a half months), and he has been a somewhat delicate child ever since. During the last four months of pregnancy the mother gained flesh and weight in a remarkable manner quite in contrast with her ill-nourished state in the early months. Some interesting articles on this placental anomaly have been contributed by Giglio (*Ann. di ostet.*, xvii. 1, 1895), Curatulo (*ibid.*, xix. 505, 1897), Ferroni (*ibid.*, xxi. 627, 1899), and many others. It is probably due to abnormalities in the formation of the decidua reflexa.

Other placental anomalies, such as adhesion to the fœtus and abnormal insertion of the cord, are rather to be regarded as morbid states of the amnion and cord than of the afterbirth itself. The literature of the whole subject is large and may be found in the *Index Catalogue*, vol. xi. p. 340, 1890.

Malformations of the umbilical cord include great length and marked shortness. Any cord measuring more than 100 cms. (about 40 inches) may fairly be regarded as teratologically long; and Taruffi (*op. cit.*, v. 195, 1889) has collected together a considerable number of records of such cases. The effect of a long cord in causing convolutions round the fœtus, and the possible effect of the convolutions in causing amputations of fœtal parts, have been already considered (p. 150). A teratologically short cord is one measuring less than 8 inches (20 cm.), and several cords with measurements of 4 or even 3 inches have been recorded (Taruffi, *op. cit.*, v. 230, 1889). Cases also are not wanting in which no recognisable cord at all was to be found, the vessels passing directly from the placenta in the membranes to the margins of an opening in the abdomen of the fœtus (*vide* under *gastroschisis*, pp. 172 and 517).

In some cases the funis ceases to have a cord-like appearance a few inches from its insertion into the placenta, and its vessels pass outwards to be attached to the fœtal surface of the afterbirth like the spokes of an umbrella; this is called the *parasol insertion* of the cord. In other cases the whole cord enters the placenta at or near to its margin, giving rise to the *marginal insertion* or *battledore placenta.* In yet other cases the cord breaks up before it reaches the placental margin, and its vessels run in the membranes for a small or great distance; this is known as a *velamentous* insertion of the cord. I have met with several instances of the two latter anomalies, both in private and in Maternity Hospital practice; they may be associated with hydramnios and with toughness of the fœtal membranes. Various more or less ingenious suggestions have been made as to the mode of production of the velamentous type of funic insertion by B. S. Schultze (*Jenaische Ztschr. f. Med. u. Naturw.*, iii. 198, 344, 1867), M. Stern (*Diss. inaug.*, Marburg, 1873), F. Ahlfeld (*Ber. u. Arb. a. d. geburtsh.-gynäk. Klin. zu Marburg*, ii. 13, 1885), and others; but there are still many difficulties in the way of a complete explanation.

I have met with at least two instances of umbilical cords containing only a *single artery.* In some cases this anomaly is due to fusion of the two umbilical arteries just inside the umbilical ring before they reach the cord, and in others it is found that the one umbilical (hypogastric) artery is much larger than the other in the pelvis, and that consequently the smaller one never reaches the umbilical ring. In yet another group of cases, however, there is complete absence of one of the arteries in the cord. This occurs specially in association with sympodia and with defective development of the bladder. The question arises whether the single artery that remains is really an umbilical (allantoic) vessel or a persistent omphalo-mesenteric (vitelline) one. There is much to be said in favour of the latter view, for the single artery is found arising from the common iliac or from the aorta itself. On this subject I have dwelt at considerable length elsewhere (*Trans. Edinb. Obstet. Soc.*, xxiii. 54, 1898).

The arteries in the cord may unite together so that only one arrives at the umbilicus of the fœtus, or they may form an anastomosis in the cord. The *umbilical vein* is rarely anomalous, but some cases are on record in which it divided into two in the cord. Its mode of termination within the abdomen is not always normal, for it may pass into a tunnel in the liver caused by the conversion of the longitudinal groove into a canal, or it may open into the vena cava inferior, or into the iliac or splenic veins, or even into the vena cava superior or the right auricle.

In rare cases the *omphalo-mesenteric* or *vitelline vessels* may be found in the cord of the full-time fœtus, and may be seen passing to a persistent umbilical vesicle on the fœtal surface of the placenta. By close inspection I have several times found traces of the umbilical vesicle in the full-time placenta, generally in the situation indicated by the direction of Schultze's fold; but I have only met with one case in which the vitelline vessels were present in the cord. The placenta is figured in Vol. I. of this MANUAL (p. 155). There were four accessory vessels in addition to the two umbilical arteries and the vein, and these four vessels (two arteries and two veins) were apparently carrying blood up to the time of birth. Unfortunately the state of the abdominal blood vessels in this infant was not ascertainable. The *literature* of anomalies of the umbilical cord and its vessels is to be found in the *Index Catalogue*, vol. xiv. 948, 1893; the whole subject, also, is treated in a masterly fashion by Taruffi (*op. cit.*, v. pp. 188–271, 1889).

With this short sketch of the anomalies of the placenta, cord, and vitelline vessels I bring to a close the long series of malformations which may affect various regions and structures of the body. I have not made a complete enumeration of them all, although I have tried to give some facts relating to all the more typical ones, and have generally indicated some article or book in which full details might be found. I have all along had in mind rather the illustration of general principles than the minute description of individual types; and I have specially tried to cite examples demonstrating the great principle of arrested development in the causation of the monstrosities which occur in the single fœtus. I have endeavoured to exclude any double monstrosities, for they will be referred to under Germinal Pathology; but it was not possible always to avoid some reference to such intermediate types and connecting links as polymastia, polydactyly, double penis, etc. They lie on the border line between the monosomatous and the polysomatous terata, between arrested developments and anomalies showing apparent excessive development; and it is difficult to assign to them their proper place. This remark applies also to the curious condition known as heterotaxy or transposition of the viscera; it differs from all other malformations and monstrosities in that it consists of nothing more than a reversal of the right and left sides of the body; it is not certain whether it is due to causes acting on the embryo as it is formed in the embryonic area, or to influences coming into play earlier and affecting the germ. At any rate, I place its consideration immediately after the monosomatous terata, between them and the double monsters and other morbid developments of the germinal epoch.

CHAPTER XXX

Heterotaxy or Transposition of the Viscera: Definition, Synonyms, Historical References, Literature, Illustrative Cases, Morbid Anatomy, Varieties (Total, Partial, Irregular), Associated Malformations, Transposition in Animals and in Double Terata, Clinical Aspects, Diagnosis, Prognosis, Teratogenesis: Antenatal Diagnosis of Monstrosities: Retrospect and Conclusions.

Heterotaxy.

Heterotaxy may be *defined* as that congenital anomaly in which the relation of the parts of the body is so altered that the organs which ought to be on the right side are found on the left, and conversely. There is an inversion of parts as in a mirror, so that if, in such a case, the thoracic and abdominal cavities be laid open their contents appear as if seen in a glass. There is, therefore, not simply the presence of right side organs on the left side and *vice versâ*, but organs which are single and median in position have their normal asymmetry so changed as it would be when reflected by a mirror.

Heterotaxy has various *synonyms*, including "transposition," "inversion," and "lateral inversion of the viscera," "situs viscerum inversus," "situs mutatus," "situs partium perversus," "dislocatio viscerum lateralis," etc. "Transposition," "inversion," and "dislocation" are not very exact terms, for they convey the idea of an actual displacement of parts such as does not occur; under the circumstances the most satisfactory term is *heterotaxy*, introduced by I. G. Saint-Hilaire in 1836 (*Histoire des anomalies*, ii. p. 3, 1836); this name, being derived from τάξις, *arrangement*, and ἕτερος, *different*, simply means an irregular disposition of parts. It has been subdivided into *total* heterotaxy, when all the body-cavities and their organs are transposed, and *partial* heterotaxy, when only the thoracic or the abdominal viscera show the changed relations.

Historical references to cases of heterotaxy go back as far as the time of Aristotle, who clearly observed it in animals, stating that he had found the liver on the left side and the spleen on the right. The references are in his *History of Animals* (Bk. i. c. xiv. par. 5; Bk. ii. c. xii. par. 4), and in his treatise on *Generation* (Bk. iv. c. iv. par. 3); and he went on to declare that this displacement might occur in animals otherwise normal. A long silence followed Aristotle's statement, and then, in the seventeenth and eighteenth centuries, cases began to be reported, but almost always as the result of post-mortem examinations. This need cause no surprise, for the anomaly consists solely of the displacement of internal organs; and it was not till the nineteenth century, when physical diagnosis by percussion, auscultation, and skiagrams began to be perfected, that the recognition of such internal abnormalities became possible during life.

Marie de Medicis, wife of Henry IV. of France, and mother of Louis XIII., is believed, on the authority of the younger Riolan (1649), to have been the subject of transposition of the viscera, for her heart beat on the right side; but it is possible that the anomaly had been acquired. Perhaps this case may have been in Molière's mind when he wrote the famous passage in *Le Médecin malgré lui* (Act ii. sc. vi.): Géronte says to Sganarelle, "On ne peut pas mieux raisonner, sans doute. Il n'y a qu'une seule chose qui m'a choqué: c'est l'endroit du foie et du cœur. Il me semble que vous les placez autrement qu'ils ne sont; que le cœur est du côté gauche, et le foie du côté droit." Sganarelle replies, "Oui, cela etait autrefois ainsi; mais nous avons changé tout cela, et nous faisons maintenant la médecine d'une méthode toute nouvelle." On the other hand, it is possible that he may have heard of the criminal with situs inversus dissected by Bertrand in Paris in 1650. The reader will find the whole question of the relationship of Molière's allusion to these two cases fully discussed by Taruffi (*op. cit.*, viii. 153, 1894). Morand's observation was made upon a man, seventy-two years of age, and has often been attributed to Méry, who communicated it to the Parisian Academy of Sciences; it created much interest and was celebrated in such poetical effusions as the following:

> "La nature, peu sage et sans doute en débauche,
> Plaça le foie au côté gauche,
> Et de même, *vice versâ*,
> Le cœur à la droite plaça."

An instance of "the order of all the bowels inverted" was reported in England by H. Sampson (*Philos. Trans.*, iii. 111, 1700) towards the close of the seventeenth century; and since then there have been several hundreds of observations made in different parts of the world by various medical men. Taruffi (*op. cit.*, v. pp. 507–549, 1889; viii. 148–182, 1894) gathered together over two hundred references, and the *Index Catalogue* (vol. xv. 775, 1894) contains many more; in 1897, I made a digest of recent literature on the subject, analysing forty-five cases reported during the years 1894, 1895, 1896, and 1897 (*Scott. Med. and Surg. Journ.*, i. 1020, 1897).

I have seen one case, that described lately by Sir Thomas Fraser (*Scott. Med. and Surg. Journ.*, xv. 160, 1904); and in 1898 Dr. David Landsborough wrote to me describing three instances of inversion which he had seen in natives of Formosa. Dr. Landsborough's patients were two men and a boy; and in all of them the anomaly was discovered in the same way. I quote from his letter. "A very large number of my patients suffer from chronic malaria, and come complaining of a 'hard lump in the side of their abdomen' (that is about the translation of what they say). On asking where exactly the hard lump is, they usually place their hand on the left lumbar region. In the three cases I have referred to, the patients indicated the *right* side, and, on placing my hand there, I felt at once a hard firm tumour, with notched border, disappearing under the angle of the ribs, exactly like a spleen. On passing the hand up to the mammary region, the heart was to be very distinctly felt beating on the right side, while not the slightest pulsation could be felt on the left side of the chest. Auscultation and percussion confirmed the impression that the heart was transposed. There were no signs of disease in either lung which could have produced any change in the position of the heart. The liver could be distinctly percussed out on the left side in a position exactly corresponding to its normal position on the right. In the case of the boy, a rough loud systolic murmur was heard all over the præcordia, most distinct over the transposed pulmonary area, probably due to congenital stenosis of the pulmonary orifice." I have quoted from Dr. Landsborough's letter to emphasise the importance of watching for cases of transposition of the viscera in malarial countries where the splenic hypertrophy is an aid in diagnosis.

The *morbid anatomy* of heterotaxy is interesting chiefly on account of the perfect way in which the transposition has been carried out, if I may use a somewhat inexact manner of speaking, for there is no reason to believe that any transference of parts from one side of the body to the other occurs.

In the thorax, for instance, the œsophagus passes from the middle line towards the right half of the diaphragm, and describes two curves, the upper with its concavity to the left and the lower with its concavity to the right. The right lung has two lobes and the left three; and the bronchi also are inverted. The axis of the heart and pericardial sac is directed obliquely downwards and to the right; and about two-thirds of the organ lie to the right of the middle line and only one-third to the left. The cardiac apex lies in the right mammillary line, corresponding to the fifth rib or the fifth intercostal space. The pulmonary veins open into the right auricle, and the corresponding ventricle gives origin to the aorta; the left auricle receives the blood from the superior and inferior cavæ and from the coronary veins, while the left ventricle sends it on to the lungs in the pulmonary artery. On account of the functional changes involved in this inversion, the right ventricle develops thick walls and the left has thin; but this character is not marked at birth. A two-segmented valve divides the two chambers of the right heart, while a three-segmented one is interposed between those of the left heart. The pulmonary artery arises from the left ventricle and passes obliquely to the right; it divides into two branches in the concavity of the arch of the aorta, the shorter of which goes to the right lung and is connected with the ductus arteriosus. The same inversion affects the aorta both in its arch and in its descending part, the great vessels which arise from it, the great veins, the thoracic duct, the phrenic, pneumogastric, and sympathetic nerves, and the smaller vessels of the thorax. The diaphragm also exhibits similar changes, those openings in it which are normally on the left side being found on the right, and *vice versâ*; and its level on the left side is higher than on the right.

In the abdomen, the stomach is found on the right side where its greater part occupies the right hypochondriac region; its pyloric end is placed in the epigastrium; and the whole organ has a direction from above downwards, from before backwards, and from right to left. The duodenum has its concavity facing the right; it is directed upwards, to the left, and backwards, and then turns vertically downwards and proceeds from left to right to become continuous with the jejunum; thus its three portions are situated in the left half of the abdominal cavity. The large intestine, from the cæcum (and appendix) to the sigmoid flexure and first part of the rectum, is exactly transposed, the cæcum being on the left side and the sigmoid flexure on the right. The pancreas has its head or larger end to the left, and its tail to the right side, and lies in the concavity formed by the inverted duodenum. The spleen is on the right side, while the larger lobe of the liver is on the left and the smaller lobe comes into relation with the stomach on the right side. The gall bladder and ducts are on the left side. The right kidney is at a higher level than the left, as is the right suprarenal capsule as compared with the left. The right ureter is longer than the left; the right testicle hangs lower than the left; and the uterus faces slightly to the left instead of to the right. The abdominal aorta, the portal vein, and the vena cava inferior, as well as the other vessels, are all exactly inverted.

Even in the cranium there are signs of inversion. The right half of the brain is larger and weighs more than the left; and the venous sinuses, as regards their size, also exhibit inversion (Calori, *Mem. Accad. d. sc. d. Ist. di Bologna*, 4 s., ii. 597, 1880). This is also evident when the cerebral arteries, and the fossæ of the cranium, and even the lachrymal sacs are closely examined. It is said that the hair on the head also has a vertex directed from left to right instead of from right to left.

Such are the appearances found on dissection in cases of complete transposition of the viscera. I have not gone minutely into details, but the reader who may desire more exact descriptions will find them admirably set forth by G. F. H. Küchenmeister in his fine monograph of 367 pages (*Die angeborne vollständige seitliche Verlagerung der Eingeweide des Menschen*, 2nd edit., Leipzig, 1888).

Transposition of the viscera has not always a morbid anatomy so complete and exact as that described above: there are cases which must be called incomplete, partial, or localised. For instance, the heart alone may be affected, giving rise to the state known as *dexiocardia*, a comparatively rare occurrence, and not to be confused with cardiac displacement due to disease. There may be simply a transposition of the great vessels, the heart remaining on the left side of the body, but this is hardly to be considered here; it has been described along with the malformations of the heart, with which, indeed, it is generally combined. Apparently the lungs are hardly ever transposed without the other organs sharing in the change;

while, on the other hand, the other viscera may be inverted without the participation of the lungs. Some of the abdominal organs, perhaps all of them, may be transposed without there being any changed relations in those of the thorax.

All writers are by no means agreed as to these atypical cases of transposition. Lochte (*Beitr. z. path. Anat. u. allg. Path.*, xvi. 189, 1894), in a learned article, states his belief that no instance has yet been put on record in which clearly marked situs transversus of the organs of one body-cavity was accompanied by an entirely normal arrangement of those in the other cavities. Apparent exceptions to this law may exist, *e.g.* Auché and Bouyer's case (*Journ. de méd. de Bordeaux*, xxvii. 413, 1897); but these are, as a rule, founded on the results of clinical examination only, and are, therefore, not free from possible errors. Situs inversus of the thoracic organs is either part of a general transposition, or is the accompaniment of anomalies in the distribution of the great veins of the abdomen or in the position and appearance of some of the abdominal viscera. The inverted position of single organs (*e.g.* stomach, liver, and heart) is not to be regarded as directly related to the causes of situs transversus, but is to be ascribed to local anomalies in development, and these local anomalies, there is good reason to believe, belong to a later stage in embryological formation. This is the probable explanation of such a case as Launay's (*Bull. Soc. anat. de Paris*, lxix. 320, 1894): in the body of a woman who had died from cancer of the pancreas all the organs of the anterior and posterior mesogastrium were transposed; all the other abdominal and thoracic viscera were normal in position, as were also the aorta, the vena cava inferior, etc. This occurrence may be explained by imagining an inverse rotation of the mesogastrium, so that the right surface thereof, instead of the left, becomes anterior.

Associated malformations may occur along with transposition of the viscera. There may, for instance, be structural anomalies of the heart; thus, in H. Jellett's case (*Lancet*, i. for 1897, p. 878), there was a tricœlian heart, two auricles opening into a common ventricle; and other instances were reported by Valleix (*Bull. Soc. anat. de Paris*, ix. 253, 1834), L. Vincenzi (*Arch. per le sc. med.*, Torino, ix. 283, 1885–86), and many more. The spleen also may be malformed as well as misplaced, the commonest anomaly being division into two or more lobes or separate parts (Marchand, in Ahlfeld's *Ber. u. Arb. a. d. geburtsh.-gynaek. Klin. zu Giessen*, 1881–82, p. 254, 1883; Launay, *loc. cit.*; Hyrtl, *Handbuch der topographischen Anatomie*, i. 492, 1847). Bifidity of the thumb has been noted (J. P. Boyd, *Glasgow Med. Journ.*, xliv. 89, 205, 1895; Sir Thomas Fraser, *loc. cit.*); the vena cava inferior has been seen uniting with the vena cava superior before entering the heart (A. M. M. Whinnie, *Lond. Med. Gaz.*, xxvi. 31, 1840); absence of the right kidney and suprarenal capsule has been observed (Beaufumé et Caron, *Bull. Soc. anat. de Paris*, p. 1006, 1902); and the thymus gland was found persisting at the age of thirty-five (A. Pic, *Prov. méd.*, Lyon, x. 535, 1895).

Although Aristotle so long ago pointed out the occurrence of visceral transposition in animals, very few modern instances have been reported. Transposition of the heart, however, has been observed in the embryos of birds, more especially in instances of artificial incubation (Dareste, *op. cit.*, 2nd edit., pp. 338–355, 1891). In other animals, more especially in invertebrates which show marked asymmetry, a state of affairs is found which may be grouped with transposition of the viscera. It consists in a reversal of the usual twisting or asymmetry of the whole body, and is seen, for instance, in some gastropods among the mollusca, and in some pleuronectidi among the teleostean fishes. Saint-Hilaire (*Histoire des anomalies*, ii. 23, 1836) called this *general inversion*, to distinguish it from the *internal* or *splanchnic inversion* seen in the human subject, and grouped them both under heterotaxy; but it is evident that there is no clear distinction, for even in the human subject signs of external inversion (difference in height of the testicles) may be seen if closely looked for, although, of course, they are not so obvious as in a one-sided shell or a flattened fish.

The relation of situs inversus to twins and double monsters raises complicated questions and problems in teratogenesis. It was stated by Förster, and some observations seem to confirm the view, that the right twin in double monsters showed transposition of the viscera, while the left-sided one showed the usual arrangement (situs solitus). But many double terata have been described in which there is no such inversion in the right hand individual; indeed Taruffi (*op. cit.*, v. 554, 1889) had difficulty in collecting together from literature ten instances of double monsters exhibiting transposition. Sometimes, however, as in one of R. J. Berry's cases (*Trans. Edinb. Obstet. Soc.*, xxviii. 222, 1903), there is a partial inversion of the great vessels in the right hand twin. Complete situs inversus must, therefore, be looked upon as only an occasional complication of the double terata. Similarly in separate twins it is a rare occurrence. Baron (*Rev. méd. franç. et étrang.*, i. 323, 1826) noted such an exceptional case, and W. B. Hadden (*Lancet*, ii. for 1890, p. 1156) recorded another. Neither in triplets nor in quadruplets would situs inversus appear to be common (Küchenmeister, *op. cit.*, p. 223, 1888).

In its *clinical aspects*, transposition of the viscera is full of interest, although it must be confessed that the interest is postnatal rather than antenatal. There is no evidence that the anomaly is transmitted by heredity; even cases of family prevalence are very rare, E. Rogi's observation on a brother and sister (*Sperimentale*, xlv. 376, 1880) being almost unique. It is of more common occurrence in men than in women (twice as common in the cases I have analysed); but, of course, there are accidental circumstances which may partly account for this. It has seldom been noted at birth, save in infants stillborn or otherwise deformed; only about twenty-one of the cases in Taruffi's long list of over 200 references were new-born infants. It may be first noticed at any age, for it may give rise to no inconvenience and to no symptoms, and it is indeed usually discovered quite by accident, either by the individual himself or by the physician, during examination for life assurance, or military service, or for a slight ailment. It is questionable whether the anomaly reduces the probability of a long life to a point below the normal. In a few cases the patients have been described as delicate; in Barié's case (*Bull. et Mém. Soc. méd. d. hôp. de Paris*, 3 s., xi. 486, 1894) and in Hayem's (*Méd. mod.*, vi. 397, 1895) there was cyanosis, but this may have been due to an associated malformation. The inversion of the organs is generally so complete that the physiology of the organs is not interfered with; since every organ is inverted, the functions of the whole organism are normally performed. Procreation is unimpaired.

There are, however, two or three functional peculiarities which have been occasionally found associated with this visceral anomaly. One of these is left-handedness. The association is far from being constant, but it is noted rather more frequently than among individuals with situs solitus. Among recent instances those of R. Caton (*Journ. Anat. and Physiol.*, xxxi. 446, 1896–97) and A. S. Warthin (*New York Med. Journ.*, lix. 306, 1894) may be cited; and A. N. Blodgett's patient was ambidextrous (*Boston Med. and Surg. Journ.*, cxxxiv. 213, 1896), while Galinsky's, although right-handed, unconsciously wrote "mirror-writing" with his left hand (*Jahrb. f. Kinderh.*, xxxix. 91, 1894). One of Posselt's patients, although right-handed, had greater power in his left hand, as shown by the dynamometer (*Deutsches Arch. f. klin. Med.*, lvi. 202, 1895).

Another function upon which transposition of the viscera may possibly have an influence is child-birth. Cases in which women with visceral transposition have given birth have seldom been noted with any degree of accuracy, and K. Bodon's observation (*Centrlbl. f. Gynäk.*, xxi. 592, 1897) is therefore specially important. He noted in his patient that during pregnancy the fundus uteri lay to the left of the middle line, and was rotated so that the anterior surface faced also towards the left as well as to the front, and the right upper angle of the uterus lay in front of the left. The uterus was, therefore, inverted like the other viscera, and Bodon looked for the cause in the presence of the sigmoid flexure in the right instead of in the left iliac fossa. Perhaps, however, the most important feature in the case was the presentation of the infant with its head in the second occipital position (R. O. A.), and its birth by the mechanism peculiar to that position.

The *diagnosis* of transposition of the viscera is not difficult if attention is directed towards the chest and abdomen. At birth it may be suspected if the cardiac impulse is seen on the right side of the thorax; but it must be borne in mind that this sign is common to transposition of the viscera and to diaphragmatic hernia (left-sided) with displacement of the heart. In a case of hernia of the diaphragm (p. 478), which I met with some years ago, I was in doubt as to which of these two anomalies was present until the thorax was opened into. By means of percussion, auscultation, mensuration, and skiagraphy the physical diagnosis can generally be carried out with great exactness. By percussion it can be determined that the cardiac, hepatic, and splenic areas of dulness are exactly transposed; palpation shows the apex beat in the position on the right side of the chest that it should occupy on the left; and auscultation will demonstrate a transposition also of the cardiac sounds. Further, preliminary gaseous distension of the stomach by Frerich's method, followed by percussion and by auscultation during percussion will reveal that viscus lying to the right of the middle line, with its cardiac end to the right and its pyloric to the left, and with its greater curvature directed downward and to the right. Auscultation over the spine during deglutition will elicit œsophageal gurgling to the right instead of to the left side of the vertebral column; and palpation over the posterior aspect of the thorax will show more marked vocal fremitus on the left side, pointing to the presence of the bronchus with the greater lumen on that side. The abdominal aorta may be felt pulsating to the right instead of to the left of the spine, and inflation will show that the rectum and sigmoid flexure turn to the right side instead of to the left. Palpation and percussion may detect the cæcum in the left iliac fossa; sometimes mensuration has shown cranial and thoracic asymmetry of an unusual kind, the left side giving greater measurements than the right.

While transposition of the viscera may have no prejudicial effect upon the life and health of the individual, it may prove an awkward complication in surgical procedures. It is easy, for instance, to understand how the success of a colotomy (for intestinal obstruction) might be imperilled by its non-recognition by the operator. In the performance also of an œsophagotomy, of paracentesis thoracis, and of operations on the liver, gall-bladder, stomach, pylorus, and spleen, the presence of situs inversus would necessitate changes in the mode of procedure (Küchenmeister, *op. cit.*, pp. 176–195).

The *teratogenesis* of situs inversus is not yet fully understood, although some light has been thrown upon it. It is interesting to note that there is now a tendency to carry the time of the production of this anomaly back to the germinal period of antenatal life, or at least to the very earliest stage of the embryonic epoch; in this respect modern science differs little in theory from the views held by Winslow in the middle of the eighteenth century (*Mém. de l'Acad.*, Ann. 1733, p. 374), for according to them the transposition was due to a primitive malformation of the germ.

At first it was thought by Serres (*Recherches d'anatomie transcendante et pathologique*, art. xv. p. 108, 1832) and his followers that, in assuming their permanent position in the body cavity, the viscera were related to each other, and moved in some fashion like the planets in respect to each other and to the sun. The liver was regarded as the viscus whose position and movements determined those of the other organs; and, in inversion, it was supposed that the liver was displaced and that the other viscera simply followed. It was supposed that one of united twins always showed this inversion, and that this was due to the relationship of the two livers. Virchow (*Arch. f. path. Anat.*, xxii. 432, 1861) carried the theory a little further, and regarded the kind of torsion found in the umbilical cord as the determining cause of the position occupied by the liver and consequently by the other organs also. Facts, however, did not fit themselves to theories, and it was not long before it was found that the torsion of the cord might be left or right hand, and yet no inversion be produced with either. No determining cause, therefore, was available to explain the displacement of the liver; further, inversion was found to occur before the appearance of the hepatic rudiments; further still, displacement of the liver was noted in some cases without inversion of the other organs, and all the other viscera were discovered displaced without any change in the liver. Saint-Hilaire endeavoured to relieve the difficulties of the hepatic theory by suggesting the action of special causes in preventing some organs following the lead of the liver, as it were, in cases of incomplete situs inversus: he adduced an anomaly to explain why another anomaly did not always exist in just the same anomalous way (*Histoire des anomalies*, ii. 16, 1836). Serres' theory was further weakened by the fact that inversion of the viscera in one twin (in cases of double terata) is far from constant. Its author, however, aided progress by pointing out the primitive duplicity of many embryonic organs (*e.g.* the heart), and by showing that their asymmetry was due to more rapid growth of one half or to delayed growth or atrophy of the other.

There is another theory of the origin of heterotaxy which has gained a great amount of support. It proceeds from the observation that, in the case of the chick, the embryo lies upon its left side, and goes on to state that if it were to rest on the right side instead there would be inversion of the viscera. It has in its favour some facts in Comparative Embryology. Von Baer of St. Petersburg (*Ueber Entwickelungsgeschichte der Thiere*, i. p. 51, 1828) showed that rotation of the embryo, when it is in the opposite direction to the normal, is accompanied by inversion of the cardiac curve; and E. d'Alton (cited by Taruffi, *op. cit.*, v. 559, 1889) found an embryo chick of five days in which the anterior part of the body was rotated inversely and the heart was inverted, while the posterior part was rotated normally. The latter author further believed that in the case observed by him the chick would have developed situs inversus of the thoracic and situs solitus of the abdominal organs. This idea seemed also to agree with the supposed inverted state of the viscera in double monsters, for one could imagine the right twin lying on its left side and so having its heart and aorta inverted. The moment, however, that the developmental details begin to be scrutinised, difficulties appear in the way of a complete acceptance of the theory that curvature of the heart-tube is due to the position of the embryo on the embryonic area. In fact, the cardiac curve may be present before the rotation of the embryo takes place. Further, embryos with abnormal rotation have been found showing no inversion of the viscera, and traces of inversion have been discovered in those showing no abnormal rotation on the embryonic area. Evidently, therefore, the position of the embryo is not the determining cause. Some very ingenious suggestions have been made (by Rindfleisch and others) regarding the effect of the circulating blood on the character of the curvature of the heart; but it is unnecessary to linger over them, for it has been shown, in the case of the chick at least, that the cardiac curve is present before the circulation begins.

Dareste's theory of the cause of inversion of the viscera in the chick demands some consideration (*op. cit.*, p. 351, 1891). He pointed out that the heart is constituted by the fusion of two lateral halves; usually the right half is the larger, and so the normal curve of the cardiac tube is towards the right; but if the left half be larger then the curve will be inverted. He brought forward as proof of this view the fact that in cases of inversion in the chick the left half of the vascular area was larger than the right. He was able by unequally heating the egg to produce artificially this inequality of the two halves of the vascular area; but, unfortunately for complete proof, he did not always obtain inversion of the heart under these circumstances. Of course this result may have been due to defects in the apparatus used for carrying out these experiments. The experiments of Warynski and Fol (*vide* p. 214 of this volume) seemed to support the idea that unequal heating might retard or increase the growth of one part of the vascular area and so lead to heterotaxy; but, even more than Dareste's methods, they contained possible fallacies, due particularly to the violence of the means employed to influence the chick. Dareste's theory, however, to some extent suited the facts, and it explained in a feasible fashion how one of double twins had inverted viscera; for the proximity of united embryos would cause a dwarfing of one half of the vascular area of each, and in the case of one embryo it would be the half whose diminution led to inversion of the heart. Unfortunately, as I have already pointed out, all arguments strengthened by references to inversion in double monsters are really weakened thereby, for such inversion is inconstant; indeed it is rare.

Taruffi (*op. cit.*, v. 579, 1889) still is of opinion that in some way or other the size of the two parts of the vascular area, in the case of the embryo chick, is concerned with inversion of the viscera. There is an asymmetry of the two halves of the vascular area and of the vessels coming from it to the embryo, and this asymmetry precedes both the curving of the cardiac tube and the turning of the embryo on to its side. In inversion there is an inverted relationship of the vessels in the vascular area. The theory, therefore, goes back to the cause of the inequality of the two parts of the vascular area, to the reasons why the embryo lies on the vascular area in just the way that it does in normal cases and in a different way in inversion. There may be a reversal of the polarity of the ovum leading to an inverted cleavage. But the "orientation" of the embryo, as it is called, is still an unsolved problem both in normal and abnormal circumstances. The important fact to bear in mind, however, is that probabilities point to the origin of inversion of the viscera in a very early period of antenatal life, in the pre-embryonic or germinal epoch.

The teratogenesis of heterotaxy must, then, be left in a most unsatisfactory position; but the following facts or ideas are worth remembering. In the *first* place, it is doubtful how far it is wise to draw deductions from observations and experiments on the hen's egg. There are important differences in the ontogenesis of the mammalian as compared with the avian ovum and embryo, and these complicate the question greatly. Féré (*Compt. rend. Soc. de biol.*, 10 s., iv. 246, 1897), it is true, succeeded in producing heterotaxy (along with other monstrosities) in the chick by injecting hydrocyanic acid into the egg before incubation; but his experiments do not reveal the cause of the inversion so much as the early date of its occurrence; they are of value rather in showing that heterotaxy may apparently be determined by poisons acting on the organism in the germinal period. In the *second* place, the idea that an individual with inversion of the viscera is the right-side survivor of uniovular twins, although a most fascinating one, is not supported by facts. For instance, the much-talked-of visceral inversion of one individual in double monsters has been shown to be rare, while in ordinary uniovular twins both individuals usually show a normal arrangement of the internal organs (*situs solitus*). Again, if this theory were correct, we ought to find some trace of the twin with normal internal organs at the birth when an infant with transposed viscera is born; but as a matter of fact the expulsion of a fœtus papyraceus along with an infant with heterotaxy has not been recorded (Galinsky, *loc. cit.*). I do not, however, place much value on the latter objection, for, theoretically, the death of the twin embryo with situs solitus would be so early that no recognisable trace of it would be left. In the *third* place, a theory of heterotaxy, to be satisfactory, ought to include an explanation of the partial cases of transposition in which the heart alone, or one or other of the abdominal organs alone, is displaced. In the *fourth* place, it is useless to look for causes of heterotaxy in late embryonic life; to do so is only to introduce endless difficulties. To understand, for instance, how displacement of the heart is associated with inversion of the abdominal viscera, it is necessary to carry the mind back to the time, before the development of the diaphragm, when the organs of the thorax and abdomen are closely associated together. In the *fifth* place, there is reason to believe that heterotaxy is determined by causes acting on the organism in the germinal or pre-embryonic period, just as it seems clear that the normal asymmetry of the body is also decided at this early epoch. Possibly the cause or causes (toxic, toxinic, or other) act by causing irregularity of growth of the embryonic annexa (amnion, umbilical vesicle, chorion), by thus altering the usual relations which the embryo bears to its surroundings, and by influencing the rate of growth of its two sides. In its essence heterotaxy may be conceived as consisting of an excess of development and growth on one side of the body and of a deficiency on the other side, with this peculiarity that the side with excess is that which in normal circumstances shows deficiency, and *vice versâ*. Finally, the reader will easily perceive from what has been stated, why it is that transposition of the viscera is placed here at the end of the monstrosities of the embryo, between them and the morbid states of the germ. It is also evident how it is linked on to such states as hemi-hypertrophy, for it is essentially a unilateral inequality of growth; in transposition of the viscera, however, there is in addition a resulting inequality of development or ontogenesis. On account of its complicated relationships as well as by reason of its perplexing teratogenesis it is obviously appropriate for heterotaxy to occupy a position on the boundary line between the morbid states of the embryo and those of the germ.

Diagnosis of Monstrosities.

I know of no means by which monstrosities can be diagnosed during the first two or three months of antenatal life. Unless the conception be expelled in the form of an abortion sac, there is no possibility of knowing whether the embryo in it is normal or teratological; at least I know of none. In other words, monstrosities cannot be diagnosed in the period of antenatal life when they are produced, unless they are discharged from the uterine interior as miscarriages, and then, of course, their life has ceased. It is none the less important to examine minutely all abortion sacs. When it is remembered that we possess so few records of carefully examined monstrous embryos in the human subject, the importance of scrutinising every abortion sac becomes clear; and when it is further realised that the nearer the monstrosity is to the period of its production, the more valuable it will be for the elucidation of the problem of its causation, it becomes imperative that all such material should be utilised.

It is when the monstrous embryo has grown into a monstrous fœtus, when, in other words, the later stage of pregnancy has been reached, that the possibility of the formation of a diagnosis (without the interruption of the gestation) may be entertained. Even then it must be regarded as a matter of the greatest difficulty in the present state of our knowledge. The antenatal diagnosis of monstrosities must therefore be done, if it is to be done at all, when the unborn infant is in the fœtal period of its life. For a full consideration of the possibilities of diagnosis at this time, the reader is referred to the first volume of this MANUAL (pp. 430–448). I deal there mainly with the detection of fœtal *diseases*, but I allude also to the discovery of *monstrosities*. I need not, therefore, repeat here what has been discussed at length elsewhere; but, at the same time, I trust that the reader will re-peruse the passage referred to.

Retrospect and Conclusions.

If the reader will now pause for a moment and cast his glance backwards over the long series of monstrous types that have been set forth in the preceding chapters, he cannot fail to be impressed with the fact that underlying all the diversity there has been a singular degree of resemblance. With some few exceptions, it has been possible to see in the monstrous state of the full-time fœtus the persistence of an earlier and a normal arrangement of parts. What, however, is normal in the third week of antenatal life is abnormal at the ninth month; nay, it is already abnormal at the fourth week. In the ceaseless progression of the human organism towards the wonderful completeness and the marvellous perfection of the new-born infant, the slightest delay in the developmental processes and the smallest persistence of transitory structures constitutes an anomaly, a malformation, or a monstrosity, which, in a small degree or in a great one, interferes with the life, health, happiness, and usefulness of the individual, or with his capacity to play his part in propagating the race. A hesitation in the forward progress of ontogenetic processes is sufficient to endanger the successful development of the individual; an actual arrest produces irreparable damage. But there is a hopeful aspect of this depressing picture of the origin of antenatal deformity: arrested development must be due to an arresting cause; that cause must act at some time or another in antenatal life; it must, therefore, be possible at some time or other to bring influences to bear upon it which may check its action. If the ultimate cause is, as there is reason to believe it is, toxinic, toxic, traumatic, or microbic in its action, then it ought to be possible to attack that cause in the parents of the future offspring, for through the parents alone can it reach the child. More than this, there is an element of hope in the suggestion, supported as yet by a sadly small amount of evidence, that during antenatal life Nature is not altogether quiescent in the face of morbid states, but tries, immediately the morbid cause ceases to act, to undo the mischief that has been done and to repair the damage inflicted. The study of antenatal repair of injuries is an almost unworked field, but it offers an attractive prospect. It stands in the same relation to antenatal prevention, as, for example, the medicinal treatment of acquired syphilis does to its prophylaxis. But of all this I shall have to say some few words more after I have considered the pathology of the third and earliest period of antenatal life, the germinal; to that I now address myself.

BOOK IV

THE PATHOLOGY OF THE GERM

CHAPTER XXXI

Pathology of Germinal Life: Physiology of Germinal Life; Ovum and Sperm Production, Maturation, Fertilisation, Segmentation, Blastocyst Formation: Pathology of the Blastocyst; Hydatid Moles, Abortion Sacs without Embryos, Amniotic Defects, Heterotaxy: Pathology of the Morula Mass; Fractional Individuals, Neoplasms: Pathology of Fertilisation; Polyspermy, Double Terata, Hybridity: Pathology of Maturation; Parthenogenesis, Dermoids, Teratomata or Embryomata.

The pathology of the germ is the *Hinterland* of Antenatal Pathology. Like a great continent or island the subject lies facing the four seas. We have studied and found out much regarding its shore-line with its bays and promontories—that is Fœtal Pathology. We have also explored to some extent the difficult country lying beyond the maritime belt, without, however, attempting anything like an ordnance survey of it—that is the Pathology of the Embryo. But beyond it again is the vast Hinterland, the almost unknown interior, about which little has been definitely ascertained, although much is rumoured—that is the Pathology of the Germ.

I had hoped, when I began the writing of this book, to have considered the pathology of germinal life with the same detail as that of fœtal and embryonic existence; but to do so—to discuss, for instance, double monsters in all their varieties, to deal with heredity in all its mysterious aspects, and to investigate the antenatal origin of tumours—would require a volume and not a chapter or two. I have determined, therefore, to content myself with giving here a mere sketch, a synopsis of the subject, indicating the lines along which the discussion would have travelled had space and time permitted.

In studying the pathology of germinal life it is very necessary to bear constantly in mind one serious limitation to which it is subject—I refer to the absence of information regarding the *human* germ. Behind all the conclusions that are drawn in reference to the physiology and pathology of human germinal life, there is always the element of uncertainty arising out of the circumstance that such conclusions are mainly founded upon the phenomena of germinal activity as they are met with in the lower animals. The student of germinal pathology labours, therefore, under a very serious disadvantage—a disadvantage, nevertheless, which it is very easy to exaggerate unwarrantably. No biologist and no embryologist has ever seen the human ovum entered by the human spermatozoon, but I am not aware that the impregnation of the ovum by the spermatozoon in the human subject has, on this account, ever been denied. It is ever necessary to remember the restriction under which the investigations into germinal pathology are being carried on, but it is surely never necessary to suspend them altogether. The value of the conclusions is undoubtedly diminished, but certainly not altogether abolished.

In the study of germinal pathology, just as in that of embryonic and fœtal pathology, it is essential to begin with the consideration of germinal physiology.

Physiology of Germinal Life.

Germinal life ends, or may be said to end, with the first appearance of the rudiments of the embryo in the blastocyst. It begins, for the individual, when the ovum and the spermatozoon unite in fertilisation; but it really begins much further back, when the reproductive cells of the parents become specialised from the cells of the genital ridge. So germinal life varies in length with the age of the parents when impregnation occurs. It begins actually in the antenatal existence of the parents, stretches on through their childhood and youth till puberty, and then, when the ovum and sperm come together, passes into the life of the new organism. But inasmuch as the germ-cell is supposed to contain a bit of the structural elements of the germ of the preceding generation, and that a bit of the generation before, and so on, it becomes impossible to fix a starting-point. Must germinal life then be regarded provisionally as without a beginning? If we accept the theory of the continuity of the germ-plasm it must be conceded that it would seem so. For practical purposes, however, I consider here that the germinal life of the individual begins in the vital activities of the two reproductive cells of his parents, in the ovum and spermatozoon which by their union cause him to come into being.

A striking fact with regard to germinal life is, therefore, its primary dual character. It is at first the life of two cells, the egg-cell or ovum and the sperm-cell, but after impregnation it becomes the life of one cell, the fertilised ovum or oosperm. It will be well, therefore, to consider first the dual period of germinal existence, and the history of the ovum will be dealt with before that of the sperm, for it is the better known of the two.

The primitive ovum has been regarded as a cell of the mesoderm, one of the mesothelial cells of the genital ridge; but it may be that it is one of the original cells (germ-cells) into which the ovum divides, and that it finds its way to the genital ridge while many of its comrades lose their way, so to say, in the body tissues and disappear or perhaps form the rudiments of future tumours. In process of time it is carried into the interior of the ovary and becomes surrounded by an envelope of separate smaller epithelial cells, the whole constituting a primordial follicle. The ovum grows in size, becomes spherical or nearly so in shape; its nucleus becomes larger, spherical, and more eccentric, and the chromatin usually gathers into one nucleolus, while the achromatic substance develops into a coarse network; the corona radiata is formed, and inside it the vitelline membrane, zona pellucida, or oolemma. The primordial follicle meanwhile changes into the Graafian follicle. Before the ovum has become full grown and ready for maturation the individual in whose ovary it is resting has passed through the fœtal stage, has been born, and has reached, at any rate, the age of puberty.

By maturation of the ovum is meant the series of phenomena which occur in it just before or just after the rupture of the Graafian follicle, and the consequent separation of the ovum from the ovary; it marks the close, therefore, of what may be called the intra-glandular life of the egg-cell. There is first a centrifugal movement of the nucleus towards what has been called the *animal* pole of the ovum (in contra-distinction to the vitelline, deutoplasmic, or *vegetative* pole), and a contraction of the vitellus or yolk. When near the surface the nucleus as such disappears, and in its place is found the nuclear spindle; at both ends of the spindle are radiating threads in the vitellus in the form of a sun, and these together constitute the amphiaster. Then part of this chromatin spindle is extruded from the ovum as the first polar globule; the part that remains inside the ovum now forms a second spindle and a second amphiaster, and again a portion is expelled as the second and the smaller polar globule. These polar bodies degenerate and disappear. The remnants of the nucleus are now called the female pronucleus, and it may or may not move towards the centre of the egg-cell again, its after-history being determined by the early or late appearance of the male pronucleus. The chromatic masses or chromosomes in the ovum, originally sixteen in number in the human subject (so it is believed), have been reduced to eight. The ovum is now mature. It is the female genoblast.

The life of the sperm-cell before impregnation is not so well known as that of the egg-cell. Either from the epithelium or the stroma of the genital ridge (mesothelium), which may, as in the female, come from the original germ-cells of the ovum, are developed the solid cords which become the seminiferous tubules of the testicle. Most of the cells in the cords are small in size and epithelioid in arrangement, but here and there are some large cells corresponding to the primitive ova (*Ureier*). In fact the testis at this stage is only to be distinguished from the ovary by the comparative fewness of these primitive ova. The male sexual cords remain quiescent till puberty, when they become the seminiferous tubules in which are developed the spermatozoa. The exact method in which first the spermatoblasts and then the spermatozoa are produced is not known, but it is believed by Benda that the epithelioid cells give rise to the columns of Sertoli and the primitive ova (*Ureier*) to the spermatocytes. In a column of spermatocytes it is possible to trace a parent cell, mother cells, and daughter cells, the latter having relatively large nuclei. The spermatoblasts arise from the nuclei of the daughter cells, and from these the spermatozoa are developed by changes in the chromatin and rupture of the nuclear membrane. The spermatozoa are now ready to impregnate the mature ovum. They are the male genoblasts.

The dual period of germinal life is now brought to an end by the entrance of a spermatozoon into the ovum. Probably many spermatozoa make their way into the peri-vitelline space, but so far as is known one only normally passes through the zona pellucida and enters the yolk to form there the male pronucleus; the latter by a mechanism about which there is much mystery approaches the female pronucleus, and ultimately fuses with it to form the segmentation nucleus. Minot points out that "since the head of the spermatozoon is developed chiefly out of the chromatin of the nucleus of a spermatoblast, it follows that impregnation is essentially the addition of chromatin to the nucleus (female pronucleus) of the mature ovum." The segmentation nucleus contains as many chromosomes as the original ovum; so that fertilisation has restored the chromosomes to their previous number. It is probable that a short period of quiescence now ensues (it does so at any rate in invertebrates), and then follows the first act of combined or unified germinal life, the segmentation of the ovum.

It is unnecessary for me to enter into the details of the segmentation of the ovum, for the production of the morula mass is surely the best known of all the phenomena of embryology. It may, however, be well to bear in mind that, as Minot puts it, the regularity of mammalian segmentation is an assumption which recent researches do not warrant. Segmentation begins, to quote from Minot, when the ovum is one-half or two-thirds of the way through the oviduct; the first cleavage plane passes through the axis of the ovum which is marked by the polar globules, the two segmentation spheres are oval and subsequently become flattened against each other; the second cleavage plane is also meridional; the ovum next divides into eight, and then into twelve segments, of which four are larger than the rest; the succeeding cleavages have never been followed accurately, but it would seem that they progress with great irregularity. The segmentation being holoblastic is total, and it is believed that about this time the segmenting ovum has reached the uterine cavity. Enlargement now takes place; and, a cleft appearing in the middle of the morula mass, a cavity is gradually produced. The impregnated ovum has now reached the stage of the blastodermic vesicle, blastocyst, or blastula, or diaderm.

Let me now remind the reader of the limitation referred to in the beginning of this chapter. *We have no knowledge of what happens to and in the human ovum from the time when it is penetrated by the spermatozoon to the time when we see it, already a complex structure, as Peters found it, at the estimated age of five or six days.* It then consists (*vide* pp. 21–24 of this volume) of an extra-embryonic part, blastocyst or chorionic vesicle, covered with trophoblast (probably ectodermic in origin) and lined with a thin layer of mesoblast, which contains an amniotic sac and a pro-embryon and other things. But how has the ovum with its segmentation nucleus become converted into this complicated blastocyst? We can only hazard an opinion from the study of mammalian ova other than those of the human subject, and for this purpose Dr. Arthur Robinson's three lectures (*Journ. Anat. and Physiol.*, xxxviii. 186, 325, 485, 1904) are invaluable. It may, for instance, be conjectured that the zona pellucida is developed from the membrana granulosa and not from the ovum itself, that it may have the function of preventing the contact of the trophoblast with the mucous membrane of the tube or uterus until the ovum has reached its proper mooring-place, and it may disappear early or persist till the embryonic ectoderm reaches the surface of the blastocyst. It may also be supposed that the ectoderm develops the thick trophoblast layer during segmentation, that the trophoblast plays a very important part in fixing and nourishing the future embryo, and that therefore it appears before the first traces of an embryo. How, in the human subject, the amniotic ectoderm and the ectoderm of the pro-embryon are developed from the segmentation sphere or morula mass, and how the entoderm forms the umbilical vesicle, and whether any trophoblast cells remain inside the blastocyst, and many other matters must remain for the present quite obscure even to the skilled embryologist. The only supposition that may be hazarded is that since these structures are formed in different ways in different groups of the mammalia, they may also be constructed in yet another manner in the human subject.

The physiology of germinal life may be summarised as follows. It consists of a comparatively long period (ante-conceptional) during which it is a dual existence, an epoch in which the two parts (sperm-cell and egg-cell) are simply specialised cells of the organism (male or female) in which they lie, and in which it must be concluded that they are subject to the influences (healthy or pathological) which act upon that organism; the most noteworthy phenomenon in this epoch is the maturation of the egg-cell (expulsion of polar globules and reduction of chromosomes), and a somewhat analogous process in the sperm-cell. It consists, second, of a relatively very short period (intra- and post-conceptional), during which the mature male cell unites with the mature female cell to form a single cell, the impregnated ovum or oosperm; during this short epoch the cell thus produced becomes, by a process of division and specialisation, first the morula mass, and then the blastocyst, and lastly the blastocyst with amniotic sac and pro-embryon inside it; the most noteworthy phenomena at this time are impregnation, segmentation of the ovum, and commencing embryo-formation, and the most noteworthy structures are not the embryo (for of that there is only a trace) but the trophoblast and the amniotic sac and the umbilical vesicle.

If we ask ourselves now what is the meaning of these various processes, we plunge at once into a labyrinth of divergent opinions. There is, for instance, the question of the meaning of the sexual cells and their maturation. Perhaps Minot's theory of the genoblasts (*Human Embryology*, p. 77, 1892) explains it as well as any other, but all writers are not agreed about this. It supposes that in the reproductive cells both sexes are potentially present. To produce sexual elements the cell divides into its sexual parts, the genoblasts: in the case of the egg-cell the male polar globules are cast off, leaving the female ovum (female genoblast); in the case of the sperm-cell, the male spermatoblasts, homologous with the polar globules, multiply considerably, and their descendants give rise by further specialisation to the male elements (male genoblast), while the parent cell, or homologue of the female ovum, atrophies. In both cases the sexual cell separates into a single female element (or thelyblast), and probably two male elements (or arsenoblasts), which are capable of multiplication by division; but in one case it is the thelyblast, in the other the arsenoblast, which is preserved, differentiated further and utilised. This theory gains support from the fact that the extrusion of two polar globules seems to be common to the whole animal kingdom; its purpose would appear to be to render the ovum capable of fertilisation. It was at one time believed that in parthenogenetic ova only one polar globule was formed, that therefore part of the male element (arsenoblast) remained in them, and rendered them capable of development without fertilisation. Unfortunately for the maintenance of the above theory, this character of parthenogenetic ova has not been found to be constant.

Then, again, there is the question of the determination of the sex of the future offspring. Does it take place in the germinal period, before, during, or after impregnation; or is it settled in the embryonic epoch? This is another difficult problem. The tendency of recent research, however, seems to be to support the idea that ova are already male or female before impregnation. I have elsewhere (*Brit. Med Journ.*, i. for 1903, p. 1100) reviewed the evidence brought forward by various writers on this subject, and have shown that the probability is that the sex of the ovum depends upon the mother, and is decided before fertilisation, possibly by differences in nutrition, well-nourished ova tending to become female, and ill-nourished, male.

Pathology of Germinal Life.

If the same principle of study be applied to the pathology of germinal life as was brought to bear upon embryonic pathology (*vide* p. 73), that, namely, of looking for an explanation of morbid developments along the line of physiological peculiarities, it will at once become apparent that, theoretically, the pathology of germinal life ought to consist of anomalies in the formation of the first rudiments of the embryo, malformation of the blastocyst and of its contained parts (amniotic sac, umbilical vesicle, trophoblast), unusual modes of segmentation, errors in the details of the impregnation of the ovum by the spermatozoa, and imperfect maturation of the ovum and imperfect formation of spermatoblasts and spermatozoa. It will be shown that there is some reason to believe that what have been advanced as the probable phenomena of germinal pathology are the real phenomena. I shall discuss the pathology of the various periods in germinal life, beginning with the latest (that of the blastocyst), and working backwards towards the early time of separate existence in two sexual cells.

Pathology of the Blastocyst.

The segmentation of the ovum and the formation of the blastocyst and first traces of the embryo in it may be said to be the phenomena of the post-conceptional period of germinal life—the period, in other words, which follows the impregnation of the mature egg-cell. Now, if morbid influences act upon the new organism in this stage (blastocyst), we have to ask ourselves what the pathological results will be. Little that has definitely been ascertained can be affirmed, but some interesting suggestions may be made.

It is evident that in such a blastocyst as that figured by Peters (Figs. 3, 4, pp. 20, 21) the first traces of the embryo (pro-embryon) have only just appeared; and it may be asked what would happen if they did not appear? In answer it may be said that it has frequently been found in teratogenic experiments on the hen's egg that, if the time allowed to elapse between the laying of the egg and its incubation be too great, a blastoderm may develop without an embryo. The same thing may occur in the case of mammalian vertebrates; and from time to time one comes across abortion sacs containing no trace of an embryo. I have myself met with two cases of intact abortion sac with no embryo inside, and Giacomini (*Sulle anomalie di sviluppo dell'embrione umano*, Torino, 1889–92) has reported several. We can account for the absence of the embryo in various ways: it may die early and be entirely absorbed leaving no trace, although I am not convinced of this; it may, as Giacomini has clearly shown, be found outside its usual place in the blastoderm, and it must, therefore, be supposed that it has emigrated there (into the cœlomic cavity from the amniotic sac, or outside the chorion), or has been developed *ab initio* there; or it may never have developed at all. Under these circumstances, the embryonic annexa, as we may term the chorionic vesicle and the umbilical vesicle and amnion, may go on growing for a time and be cast off as an empty abortion sac.

If, however, the embryo fail altogether to appear, if there be an arrest prior to the appearance of the traces of an embryo, then we may ask what morbid result will follow. Some years ago I ventured to suggest that the product of such a gestation might be a hydatid mole (*Edinb. Hosp. Rep.*, vi. 366, 1900); and recent researches have gone to support this view and also to explain how it may be supposed to occur. If we imagine an early ovum, like Peters', implanted in the uterine mucous membrane, but with no embryo in it and no developing system of blood vessels, then by the continued proliferation of its trophoblast it might soon take on an appearance resembling that of the hydatid mole. Sfameni (*Giorn. ital. d. sc. med.*, Nos. 5, 6, 7, and 8, 1903; *Arch. ital. de biol.*, xl. 219, 1903–04) believes that the vesicles of the hydatid mole are neither due to dropsy nor to myxomatous degeneration of the chorionic villi, but are simply syncytial buds attached to each other by filaments; and he is able to bring forward several facts in proof of his assertion. If then the hydatid mole consists essentially of syncytium, its development from the ovum covered with trophoblast (which is the forerunner of syncytium) is not an unlikely event. When the embryo dies early, or does not appear at all, it is quite conceivable that the trophoblast may go on growing in an ill-regulated way, may bury itself in the mother's uterine wall, and so cause the typical hydatid mole. It may be objected that an embryo is sometimes found in a hydatid mole, but this occurrence is very rare, and may, when it does occur, be regarded as a twin pregnancy in which one twin is represented by the hydatid mole. Further, if we suppose that the trophoblast continue not only to grow but also to show its capacity for burrowing into surrounding tissues and invading blood vessels, we are led on to the now well-known deciduoma malignum or chorion-epithelioma. Pieces of the trophoblast or syncytium may be carried to distant parts of the mother's body and give rise to the metastatic growths. It is thus seen how a morbid state of the blastocyst may produce profoundly important effects both on the embryo itself and on its mother.

Another result of the action of morbid agencies upon the blastocyst may be the defective development of the amniotic sac and membrane. It will be remembered that these structures precede the embryo in order of development, and that the latter appears in close connection with them, as Peters' blastocyst shows. It may be that it is now that the defective development of the amnion occurs which is, according to the amniotic theory, so effectual in producing monstrosities and malformations of the embryo (*vide* Chapter XII.); or perhaps want of development of the amnion may prevent even the first rudiments of the embryo from appearing. Here, then, is the germinal factor in the production of monstrosities by amniotic action, which I referred to in dealing with the pathology of the embryo (p. 222). The state of the amnion in the germinal epoch may, therefore, determine the appearance of monstrosities in the embryonic period of antenatal life.

I have already alluded to another teratological state which may possibly be determined during the blastocyst stage of germinal life, I mean heterotaxy or transposition of the viscera. Whether there is anything in the human blastocyst which corresponds to the vascular area and its elliptical deformity in the chick is not known; but it is quite possible that the position occupied by the pro-embryon in the blastocyst, its orientation so to say, may have to do with the production of heterotaxy. Again, anomalies of the umbilical vesicle and of the mesoblastic part of the allantois may exist prior to the appearance of the pro-embryon and influence its future development; perhaps sympodia and gastroschisis may in this manner be determined in the germinal period of existence.

Much that has been said regarding the pathology of the blastocyst is speculative, but it is not unsupported by certain facts. Further, at a stage when the most prominent structures are not the embryo but what may be called its annexa, it is only reasonable to suppose that the most prominent pathological changes will be in them and not in the embryo, although the embryo may come to suffer greatly on account of them. In such a state as hydatid mole with its sequel chorion-epithelioma, the fate of the embryo is lost sight of in the danger to the mother which is produced; the embryonic annexa, by their irregular and excessive growth, produce in the mother's body the most malignant form of neoplasm to which she is liable. The trophoblast, therefore, if this view be correct, is, when normal, the great source of life to the new organism (fixing it, supplying it with nourishment, laying down the framework of the placenta), but when abnormal it brings with it death to both embryo and mother.

Pathology of the Morula Mass.

We may now inquire what pathological processes may occur in the morula mass before it becomes a blastocyst. The great phenomenon seen in the morula is segmentation; its physiological manifestation is cell division and probably to some extent cell differentiation, so that gradually the different kinds of cells seen in the blastocyst come into being. Of information bearing upon the behaviour of the morula under various morbid conditions there is no lack; but, unfortunately, it is gained from invertebrate ova and from those of frogs, and is the result of experiments which are not free from fallacy. It is difficult, therefore, to estimate how far it can be translated into the language, so to speak, of the conditions of the human morula.

Chabry, struck by the fact that in the case of ascidian ova abnormal segmentation resulting in the production of fractional embryos sometimes occurred, made the attempt to bring about the same effect experimentally. The method employed was that of injuring one or more of the spheres composing the segmenting ovum. It is well known that the first segmentation groove passes through the median plane of the future embryo, and that the second is perpendicular to the first; consequently, when there are four blastomeres, two of these represent the anterior half (made up of a right and left quarter), and two the posterior half (also made up of a right and left half). Chabry found that if he destroyed one of the two primary segments of the ovum there resulted a half-individual showing one-half of the nervous system without closure of the medullary groove. If he destroyed one of the blastomeres in the next stage of segmentation (four segments) there arose a three-quarter individual, if the two anterior cells were destroyed only the posterior half developed, if the two posterior were injured only the anterior half appeared, and, most remarkable of all, if the two diagonal cells were injured the other diagonal pair developed.

The experiments of Chabry were repeated and extended to other animal forms by several biologists, but the results obtained were most contradictory. W. Roux experimented upon the blastomeres or cleavage cells of the frog's egg. If, in the two blastomere stage, he killed one, the other developed into a typical half-embryo, an embryo that was either the right or the left half of a whole one. He concluded, therefore, like Chabry, that the first cleavage plane determined already the median plane of the adult; he thought, also, that the basis of all differentiation was given by an unequal division of the nuclear substance during karyokinesis. Hans Driesch, however, repeated these experiments (which have come to be called *blastotomy* or *blastomerotomy*) upon the sea urchin's egg, and found that the isolated blastomere cleaved like half the egg, but it resulted in a whole blastula and a whole embryo which differed from a normally produced one only in its small size. Similar results were obtained by Wilson with the eggs of amphioxus, and by Zoja with those of medusæ. Driesch went further and discovered that any one of the first eight or sixteen cells of the sea urchin's egg could develop a normal embryo; in the case of ctenophore eggs Driesch and Morgan found an isolated blastomere could develop a half-embryo, but so could a bit of protoplasm cut off from the fertilised egg before cleavage had begun. O. Schultze and Hertwig, taking the frog's egg for experimentation, were able to get either a whole embryo or a half one from one of the two first blastomeres by varying the conditions. It was thought that perhaps these different results might be due to the fact that in some cases the destroyed segment or blastomere was removed while in others it was allowed to remain; in the former case its removal may have permitted the action of post-generation, while in the latter its retention may have prevented this phenomenon.

Since the results have been contradictory it is not permissible to draw conclusions with much security. It may be said, however, that in at least some forms of life the potentiality of all the blastomeres of the segmented egg is the same; each segment may play any or every part in the future ontogenesis; Driesch, therefore, calls the whole of the segmented egg an "æquipotential system," the prospective value of each blastomere depending upon, or being a function of its position in this segmented mass. At the same time it has to be admitted that there is a degree of orientation in the segmentation mass, otherwise it is impossible to imagine why organs should be formed at one special part of it and not at another. Differentiation depends, according to Driesch, upon a "primary, innate orientation of the egg plasm in those forms, the segmented eggs of which represent æquipotential systems." Further, this orientation is capable of a sort of regulation or restoration after disturbances of any kind; but in the ctenophore egg such a regulation is apparently not possible, and in that of the frog it is possible under some conditions but not under others (facultative).

Another method of experimentation which has been used to determine the conditions of life in the stage of segmentation has been by altering the environmental conditions. Light, a sufficient temperature, oxygen, and a certain chemical constitution of the surrounding medium appear all to be essential for the growth of normal forms; while the absence or alteration of these conditions lead to anomalies. It has been found, for instance, that sulphate of quinine and chloral hydrate added to the water in which the ova of certain marine invertebrates were segmenting, caused the segmentation to begin with the tetraster stage. Gurwitsch discovered in the case of *Rana fusca* and *Bufo vulgaris* that sodium bromide and chloride and lithium chloride were teratogenic, and that the two first named when acting together produced anencephaly.

Although, therefore, there is no lack of information bearing upon the pathology of the morula stage of antenatal life, there is great difficulty in making any use of it for the purpose of elucidating the phenomena of human teratogenesis. There is this striking circumstance about human germinal life to be borne in mind that apparently the whole activity of the morula mass is, in the first place, exercised in constructing the annexa of the embryo, and that the embryo itself grows upon the annexa at a later period. Thus the whole ovum comes to consist of the trophoblast and its contained amniotic and umbilical sacs with ectoderm, entoderm, and mesoderm; apparently it is only then that the first traces of the embryo begin to appear between the amniotic sac and the umbilical vesicle. We may take it that, up to a certain stage in the formation of the blastocyst, the cells composing it are alike in appearance, and that then they assume the characters of ectoderm, mesoderm, and entoderm, and arrange themselves into trophoblast, amniotic sac, umbilical vesicle, and cœlomic cavity; but I think it would be rash to conclude, from experimental work on the ova of invertebrates and frogs, that the cells, even when they are similar in appearance, have not already their destiny fixed. Possibly the fate of the cells is to some extent determined by their position relatively to each other, but it is unlikely (although not impossible) that this entirely decides whether a given cell shall be ectoderm or entoderm, or, to carry it still further, whether it become ectoderm of trophoblast, of amniotic membrane, or of embryo. There is some probability, however, that if the cells of one part (*e.g.* entoderm) be destroyed or fail to appear, there may be an over-production of those of another part (*e.g.* ectoderm).

If we may hazard a guess concerning the results of the action of morbid agencies (*e.g.* toxic substances, microbes, toxines) upon the human ovum in the morula stage, it must be founded upon the peculiarities of the physiology of this stage. If we suppose that here again pathology takes the character of arrested development, we may imagine the morula remaining in an undifferentiated state, or having reached a later stage (*e.g.* that just before the appearance of the amnion or of the embryo), of ceasing to advance further in ontogenesis. In this way it is apparent that some of the morbid states of the blastocyst (absence of embryo, hydatid mole) may be initiated in the stage of segmentation. Further, we may perhaps suppose that some cells are arrested in their undifferentiated state, and are embedded in the midst of more progressive elements; they may thus constitute Cohnheim's rests, and give origin years later to neoplasms by a sudden resumption of activity, either of the nature of simple multiplication or of the formation of tissues of one layer of the blastoderm (*e.g.* dermoids) or of two (teratomata). Possibly, in this way, some cells of the embryonic annexa (trophoblastic, amniotic, or other) become embedded in the embryo itself, and give rise to the curious growths in the male which histologically resemble the hydatid mole and the chorion-epithelioma of the female. I think, however, I have devoted quite enough space to guesses about the pathology of the morular stage of life; but I may add one more, in relation to the causation of extra-uterine pregnancy. The trophoblast is recognised to be the means by which the ovum attaches itself to the uterine wall; presumably, then, if the ovum be detained in the tube till the trophoblast is fully formed or if the trophoblast be formed prematurely, it may effect a lodgment upon the tubal mucosa.

Pathology of Fertilisation.

The impregnation of the mature ovum by the spermatozoon is the evident phenomenon of the intra-conceptional period of germinal life. It is indeed the most important fact in all antenatal existence. Like the other great events of life, such as the birth of the infant into its extra-uterine environment and that of the embryo into the fœtal period, it is marked by an appalling mortality. It is at any rate well known that not every ovum becomes fertilised, and Balfour has stated that the whole of the spermatozoa derived from a spermatocyst are together equal to one ovum,—that is to say, eight hundred and forty-eight millions of spermatozoa. Surely I am not exaggerating when I describe such a sperm and germ mortality as appalling. Nature in this, as in her other operations where the survival of the race is at stake, provides lavishly for all emergencies; apparently many cells must die that one human being may be produced.

The physiological event of fertilisation is the entrance of one spermatozoon into an ovum; so it may be supposed that the pathological event may be the entrance of two or more spermatozoa. The physiological purpose of the act would seem to be the production of one individual from the two elements (male and female genoblasts); so the chief result of its pathology may be the production of two individuals, united directly (structurally continuous, as in the double terata) or indirectly (through the vessels of the umbilical cords, as in the placental parasites). Binovular twins arise doubtless in another way (two ova); but uniovular or monochorionic ones may be imagined as also produced by the penetration of one ovum by two spermatozoa.

The earliest theory of the origin of double terata regarded them as due to the fusion of two originally separate ova. In the case of the hen's egg, double yolks are often found, and according to this theory these ought to give rise when incubated to double monsters. This result has not been obtained by the numerous experimenters who have essayed it. A curious exception to this general experience was brought under my notice by A. H. Loeb of Montreal in 1897. Mr. Loeb sent me a photograph of a partly double chick, which I showed at a meeting of the Edinburgh Obstetrical Society (*Trans. Edinb. Obstet. Soc.*, xxiii. 53, 1898); it had a pair of supplementary legs, which seemed to have a distinct articulation slightly posterior to the normal set; and the pelvis was longer than usual. The chick, which lived two weeks, was the product of the incubation of a large egg with, presumably, a double yolk, which had been placed under a sitting hen. The circumstances of the case did not quite exclude fallacy; but the occurrence is worthy of record in face of the accumulated mass of evidence against the theory that double-yolked eggs produce double monsters.

Another theory of diplogenesis looks to fissure or splitting of an originally single embryo as the determining cause; but it is very noteworthy that experimental teratogeny has not supported this view. The production of double embryos by means of teratogenic influences acting upon an already formed embryo has not been accomplished, and it is now reasonable to suppose that the double nature of the organism is determined before the appearance of the rudiments of the embryo in the germinal area. The determining cause may be the entrance of more than one spermatozoon into the ovum in impregnation, namely, polyspermy. At the same time it is possible—theoretically possible—that it may be the existence of an ovum with two germinal vesicles; but such a phenomenon is much rarer than polyspermy, and requires after all two spermatozoa for the fertilisation of the two female nuclei. The theory of polyspermy is that accepted by Duval as most satisfactorily meeting all the requirements of the case, and it certainly affords a very good working hypothesis to account for the various kinds of double terata. At the same time it has to be borne in mind that it is largely founded upon the experiments of Fol upon echinoderm ova, and that the same results have not been obtained by other authors. Fol found that by submitting the ova to the influence of water containing much carbonic acid, two, three, or more spermatozoa entered and a complex karyokinetic figure with three or four poles in place of two resulted, and the segmentation spheres were double in number to what they were in other ova of the same age. Duval concluded that two (or more) spermatozoa united with the single female pronucleus and so produced the double development. It is now known that in some animal forms there is a physiological polyspermy which does not result in the changes described by Fol. Further, O. Schultze (*Arch. f. Entwcklngsmechan. d. Organ.*, i. 268, 1894) has in the case of frogs' eggs succeeded in getting double monsters by mechanical means (gravity) quite apart from polyspermy. It is significant and noteworthy, however, that he agrees with Duval in believing that the formation of double monsters is determined before or during fecundation. He does not think it is due either to polyspermy or to anomalies in the structure of the spermatozoa. He is therefore forced to admit that it must be caused by a condition of the ovarian ovum before impregnation, and he believes this to be an incomplete cellular division. He thinks that it is of the same nature as the formation of twins, and that in both instances we have to do not with an over-production of embryonic material, but with an arrested development.

In the presence of such contradictory results it is impossible to do more than express the opinion that the formation of double monsters is decided either before or during impregnation and not after the appearance of the embryo. It is due, therefore, to a germinal cause. I shall have something to say of the different varieties of double terata in the following chapter, as well as of the mode in which polyspermy is believed to produce them.

I have already referred (on p. 103) to another possible pathological phenomenon of the period of fertilisation, I mean the entrance of the ovum by a spermatozoon of a different species, or hybridity. It is doubtful whether this question need to be considered from the standpoint of human teratology, but it is noteworthy that Duval regarded it as a possible cause of grave monstrosities in animals. He thought that the sterility which attends the union of animals of different species may not really be due to absence of the production of an embryo, but to the production of one so grossly and intensely teratological as to be incapable of any development beyond the earliest stages. If this be so (I think it is open to doubt), there is here another teratological process taking its origin during the act of fertilisation.

Pathology of Maturation.

The terminal event of the preconceptional period of germinal life is maturation of the ovum and a somewhat similar phenomenon in the sperm-cell. There is a very considerable difference of opinion among embryologists as to the meaning to be given to maturation, but its purpose seems to be the introduction of sexuality and sexual reproduction into the life of the species. Further, sexuality may have as its object rejuvenation, the production of variability, or the prevention of variability. Now, there may exist very different views about these matters, but there can be no doubt that maturation is the preliminary condition of normal impregnation and subsequent development. It is, therefore, quite permissible to inquire what may be the results of abnormal maturation. Theoretically it would appear that the results must be teratological, and very markedly teratological; and there is good reason to believe that this is really the case.

Parthenogenesis or development without impregnation is a phenomenon met with not infrequently among the lower animal types. Several generations may be thus produced, but sexual reproduction must sooner or later intervene, and it has been noted that the individuals produced parthenogenetically become feeble and monstrous as the limit of the parthenogenetic period is being approached and the necessity for sexual reproduction becomes clamant. Now it is quite in keeping with what is known of the animal world to expect that in the higher vertebrates, and even in the highest vertebrate, an occurrence which is common among the lower forms may be met with exceptionally. As a matter of fact there is evidence that an imperfect parthenogenetic reproduction consisting in the segmentation of the unimpregnated ovum does sometimes take place in the ovary of the human subject; the result is a dermoid cyst of the ovary. Recent researches have revealed the existence of a long series of types of dermoid cysts showing all the gradations from a growth containing some hairs and skin to one containing a rudimentary but quite recognisable embryo. It is noteworthy that structures known to be derived from the ectoderm are those most commonly met with in such cysts, that parts arising in the mesoderm are less common, and that endodermic productions are extraordinarily scarce. In many cases only the parts arising from the ectoderm are present. It is clear, therefore, that here we have to do with teratological productions so monstrous that one or two of the three layers of the blastoderm are quite undeveloped; in them teratology has reached its limit. It is permissible also to conclude that the predominance of structures derived from the ectoderm is due to the fact that the ectoderm is the earliest of the layers to be formed.

It is believed that the dermoid cysts of the ovary are due to imperfect segmentation of ova that have not been expelled from their Graafian follicles. Such imperfectly segmented ova have been found in various mammals, including the Cheiroptera, and even in the human subject, especially in the case of puerperal peritonitis, where it is fair to suppose that an irritant may have excited the ovum to an abortive segmentation. The development is always very rudimentary, and may have the character of two or even three or more centres of segmentation, so to speak. In the case of the dermoid cyst described by Repin, for instance, there was found an embryo with a spinal column, a head, and four limbs, but with no intestinal canal; lying near to it, however, but not attached to it, was a cylindrical, convoluted, cord-like structure, containing a substance similar to meconium: there had been two centres of embryonic formation. This peculiarity Duval calls defect of individualisation, or apolarity of the blastoderm. Other theories have, of course, been advanced to explain ovarian dermoids (such as extra-uterine pregnancy, fœtal inclusion, and enclavement); but parthenogenesis meets the difficulties of the case best of all, for it explains how dermoids may appear before puberty, and can therefore not be due to extra-uterine pregnancy, and how they may contain teeth of the second dentition, and very long tresses of hair, for they may have lived a long time in the ovary.

A similar explanation may be advanced to account for some of the teratomata or embryomata of the testicle, for it is known that primordial ova exist in the testis as well as in the ovary, but in smaller numbers, and one of these may have taken on a parthenogenetic development. It may also be that the sperm-cell is capable of similar changes. According to this theory of ovarian and testicular dermoids, they are to be regarded as very rudimentary embryos produced parthenogenetically; they are therefore, as Duval points out, to be looked upon not as the sisters or brothers of the individual in whose genital gland they are found, but as his or her children.

Finally, it is, I think, quite in keeping with what is known of the life of the egg-cell and sperm-cell, that defects in maturation, arising perhaps from the presence of microbic or toxic substances, may be the exciting causes of the parthenogenetic segmentation. Possibly the expulsion of one polar globule instead of two, or the expulsion of none at all, may be the error in maturation ; but we are dealing with matters so debatable that speculation becomes futile, perhaps also dangerous.

Before I proceed to the study of the pathology of the reproductive cells before maturation, I must consider very briefly, synoptically in fact, the varieties of double terata and included fœtuses.

CHAPTER XXXII

Polysomatous Terata: Uniovular or Monochorionic Twins: Allantoido-angiopagous Twins; Definition, Synonyms, Varieties (Paracephalus, Acephalus, Amorphus), Teratogenesis: United Twins or Double Terata; Symmetrically United (Syncephalus, Dicephalus, Thoracopagus), Asymmetrically United, Teratogenesis: Triplets, Normal, Malformed, United: Quadruplets: Quintuplets: Sextuplets: Septuplets.

In this chapter I shall endeavour to give a short sketch of the subject of double terata. It will be nothing more than a sketch, for reasons which I have already stated; but I may add that since Taruffi gives 1650 pages out of a total of 4500 in his great *Storia della teratologia* to the consideration of double monsters, it is plain that if I were to devote a proportionate amount of space it ought to be two or three hundred pages rather than twenty or thirty. At the same time it is to be borne in mind that Taruffi deals with the double monsters in an exceptionally thorough fashion.

Polysomatous Terata.

If the reader will turn back to page 235 he will find there the various monstrosities which are usually grouped under the term "polysomatous terata." The name, roughly speaking, corresponds to the "monstrosities by excess or abundance" of other writers; and it includes uniovular (or monochorionic) twins, allantoido-angiopagous twins or placental parasites, united twins or double monsters proper, and triplets, quadruplets, and other plural births. On pages 237 and 238 I have given the leading features of these four groups; my reason for placing them here under the pathology of the germ is that I believe them all to be determined during the germinal period before the first rudiments of the embryo have appeared in the blastocyst.

Taruffi (*op. cit.*, ii. 103, 1882) grouped the monochorionic twins, the placental parasites, and the united twins together under the heading *disomata*; then he divided them rather appositely into *diæretic* and *synæretic* disomata. The diæretic are the monochorionic twins and the placental parasites, in both of which the union is not direct but indirect, a matter of diæresis, through the placenta or vessels of the umbilical cord; the synæretic are the united twins, in which the union is intimate and direct between the bodies of the twins, a matter of synæresis. Although the names are appropriate and the distinction is an important one, I hesitate to use them here on account of their unfamiliarity to the British reader.

Uniovular Twins.

Under the names of "uniovular twins," "monochorionic disomata," and "homologous twins" are described those cases in which there are twins of the same sex, which show no gross malformations, enclosed within a single chorion and provided with a single placenta. Binovular (or dichorionic) twins may be either of the same sex or of different sexes, but uniovular twins are always of the same sex. Exceptions to this rule are very rare and are capable of being explained away: the twins may be really of the same sex but one may be a pseudo-hermaphrodite. Possibly this is the reason why in veterinary practice the "free martin" is sterile, the "free martin" being the supposed cow-calf born co-twin with a bull-calf but being really a pseudo-hermaphroditic male. In the absence of exact details regarding the annexa (placenta, chorion) it is impossible to be certain about this matter. It is a striking fact that in the human subject cases in which both twins were the subject of a genital malformation have been put on record; errors in the declaration of sex were thus caused. There is no foundation for the belief that the female born co-twin with a male is sterile in the case of the human subject.

As a general rule, uniovular twins show a strong resemblance to each other. A good example of this occurred in connection with a patient who was being treated for hydramnios in the "Hamilton Bed" in the Royal Maternity Hospital, Edinburgh, in November 1901. The patient was a X-para, thirty-seven years of age, and was admitted suffering from vomiting; her abdomen was much distended, and many fœtal parts could be felt; labour came on, and when the membranes ruptured there was a great gush of liquor amnii; one twin presented by the head and the other by the breech; both twins were females and closely resembled each other in appearance; and the placenta and the chorion were single. Some cases are on record where twins had identical malformations (*e.g.* polydactyly), but it is not always possible to ascertain whether they were uniovular or binovular (Windle, *Journ. Anat. and Physiol.*, xxvi. 295, 1891–92; *Proc. Birmingham Philos. Soc.*, viii. 139, 1892).

Uniovular twins are not always of equal size, and when one dies in utero it may be expelled as a small flattened fœtus (*fœtus compressus*) along with a living full-sized infant (*vide* p. 145). It has been found, however, that the fœtus compressus may be the result of the death of one of binovular twins, so that it is not peculiar to the uniovular type. Both twins, however, may be born alive and yet differ much in size; this occurrence is probably to be ascribed to asymmetry of the circulatory relations of the twins in the placenta, and that in its turn may be due to one embryo being originally weaker than the other. This vascular asymmetry reaches its maximum in the next group of monstrosities, the allantoido-angiopagous twins.

In uniovular twins the placenta and chorion are single; but there may be, and there usually are, two amnions. In the very rare cases in which there is only one amnion, it is generally believed that the amniotic membrane between the two originally separate sacs has been destroyed. There may be two umbilical vesicles, widely separate or near to each other, or there may be only one (F. Ahlfeld, *Arch. f. Gynaek.*, xi. 160, 1877). One cord may have a central and the other a marginal insertion into the single placenta; occasionally the two cords get knotted and twisted together.

Uniovular twins are rarer than binovular, the former constituting about 12·25 per cent. and the latter about 87·75 per cent. of all twin births; about one uniovular twin pregnancy occurs in 711 single gestations. Different results, however, are obtained in different countries. The following general characters have been fairly well established for uniovular twins: there are more males than females; the mothers are apt to be young or relatively old, and multiparæ are not commoner than primiparæ; the difference in weight between the twins is often considerable; fœtal death and malformations and hydramnios are commoner in uniovular than in binovular twins; and heredity is not usually present (Rumpe, *Ztschr. f. Geburtsh. u. Gynäk.*, xxii. 344, 1891).

While binovular twins are doubtless due in most cases to the impregnation of more than one ovum, and this, again, is predisposed to by an excess of ovisacs in the ovaries (persistence of a fœtal condition); uniovular twins may be ascribed, perhaps, to polyspermy, to the penetration of one ovum by two spermatozoa, or, perhaps, to the presence of two germinal vesicles in one ovum. Polyspermy may be due to an arrest in the train of phenomena which ensue when one spermatozoon gains entrance to an ovum; it may be supposed that normally some mechanical or chemical condition prevents the entrance of a second spermatozoon, and that in abnormal circumstances this is interfered with, and so another impregnating element finds its way in. Two embryos may then appear in the blastocyst. Both in the binovular and in the uniovular twins, therefore, the ultimate cause may be an arrested development, the persistence of a state which ought to be temporary; but this is much more evident in the former than in the latter. This being so, it is permissible, I think, to call both kinds of twins teratological; but it is customary to separate the uniovular off from the others as being more clearly anomalous, and the separation may be retained although it is probably artificial.

Allantoido-Angiopagous Twins.

Allantoido-angiopagous twins are uniovular or monochorionic fœtuses which communicate with each other by means of the vessels of their umbilical cords near to or in the single placenta; one of them is usually fairly normal in structure, while the other shows an amount of deformity which is always considerable and may be extreme. They are always of the same sex. They have been called *placental parasites*; but the name is hardly suitable, for one of them (the deformed one) is really a parasite upon the other (the normal one) by means of the vessels in the placenta; they are not, therefore, parasites upon the placenta. They have been called *omphalo-angiopagous disomata* by Taruffi (*op. cit.*, ii. 133, 1882), but I prefer the term "allantoido-angiopagous" as etymologically more correct, for it is through the allantoic vessels that the communication between the twins is established. The most striking feature about those fœtuses is the degree of deformity which is reached by one of them, the parasitic one; it is in such monstrosities as the acephalic, acormic, anidean, and acardiac, that Nature attains to the extreme limit of teratological expression. Apparently, the presence in utero of *two* fœtuses makes it possible for one to assume such grotesque, bizarre, and extraordinarily aberrant forms, in which the appearance of the human embryo is nearly, if not quite, lost. Doubtless, it is through its parasitic relation to its normal brother or sister (the autosite) that the deformed twin (the parasite) is able to reach such a degree of monstrosity and yet live on in the uterus.

It has been my fortune to meet with several specimens of the allantoido-angiopagous twin, and some years ago I published a series of articles upon them (*Trans. Edinb. Obstet. Soc.*, xviii. 38, 94, 201, 257, 1892–93, xix. 41, 61, 73, 1893–94; *Teratologia*, i. 1, 25, 158, 1894, ii. 182, 1895), to which I refer my readers for details and bibliographies. Fine articles on the same subject, with literature lists, are contained in Taruffi's work (*Storia della teratologia*, ii. 133, 1882; iii. 480, 1885; iv. 137, 1886; viii. 444, 1894), and in that by F. Schatz which bears the somewhat inappropriate title of *Klinische Beiträge zur Physiologie des Fötus*.[1] I may give here the leading characters of the three chief groups into which allantoido-angiopagous deformed twins have been divided—the paracephalic, the acephalic, and the amorphous monstrosities.

The *paracephalic* twin is distinguished by the possession of a head; the other parts of the body and the limbs show different degrees of imperfection, indeed the lower limbs or the lower limbs and trunk may be absent, and the upper limbs are commonly very defective. The type which approaches most nearly to the normal is the fœtus with a more or less deformed head, a trunk, and lower limbs, with malformed or absent upper limbs, and with a heart; to this fœtus the name *paracephalus dipus cardiacus* has been given, and I have described a case in *Teratologia* (vol. i. 158, 1894). The heart, although present, is nearly always greatly malformed; it is sometimes not in direct communication with the umbilical vessels, so that for physiological purposes the fœtus might almost be without a heart. Most of the internal organs may be absent or grossly deformed. The vessels of the umbilical cord are usually defective and communicate with those of the cord of the normal twin. There must, then, be two circulations in the monster, one in connection with its own heart, and the other kept going by the heart of the co-twin through the allantoidal communicating vessels; both these vascular arrangements are doubtless imperfect, an imperfection which is the cause of the dropsical state of the subcutaneous tissue which is so commonly noticed. The two distinguishing features are the presence of a heart and the existence of two feet (dipus), although some toes may be wanting. The more common type of paracephalus dipus has no trace of a heart, hence its name, *paracephalus dipus acardiacus.* A striking example of this monstrosity I described in 1892 (*Trans. Edinb. Obstet. Soc.*, xviii. 44, 201, 1892–93): it had a fairly well formed head, but there was no foramen magnum; there was no trace whatever of a vertebral column; and the shoulder and pelvic girdles (with their attached limbs) were simply held together by a narrow bridge of muscular and adipose tissue. In fœtuses of this kind the only circulation is that (an inverted one) which is forced into them by the heart of the normal co-twin. At the same time it is very remarkable that in their morbid anatomy they so closely resemble the paracephalics with a heart.

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[1] This work, published in Berlin in 1900, consists mainly of papers reprinted from the *Archiv für Gynækologie*.

Another variety of the paracephalic twin is that in which there is only one lower limb; the single lower limb may represent two fused together (*paracephalus sympus*), or it may really consist of the right or left lower extremity (*paracephalus monopus*). In all the known specimens of this type (there are not many) there is no record of a heart; they are all, therefore, acardiac. There is usually only one artery in the umbilical cord. Another rare variety is *paracephalus apus,* in which there are no traces of lower limbs at all; the upper limbs, likewise, may be wanting. I have found records of two specimens with a heart, and of four without that organ (*Trans. Edinb. Obstet. Soc.*, xviii. 263, 1893).

Finally, there is the *paracephalus acormus* or *pseudo-acormus,* the fœtus which consists solely of a more or less perfect head and an absolutely rudimentary trunk. This type marks the extreme limit of imperfection which can be reached by the paracephalic monstrosity; the individual is reduced to a head without a body. It is no matter for wonder that for some time teratologists refused to believe in the existence of such "asomatic omphalosites" or "cephalides." The cases reported by Nicholson (*Diss. inaug.*, Berlin, 1837), Rumpholz (*Diss. inaug.*, Halis, 1848), H. C. L. Barkow (*Ueber Pseudo-akormus,* Breslau, 1854), and others are, however, so clear that doubt is no longer possible. I have met with a case which was either an acormic paracephalus or a dermoid cyst expelled per vaginam in labour; it was an osseous box, like a cranium, with a pedicle and vessels running in it. Unfortunately the placenta of the normal child born at the same time was not kept (*Trans. Edinb. Obstet. Soc.*, xvii. 49, 1891–92). The head in such cases is generally deformed; thus, in Rumpholz' specimen there was a single eye with a nasal projection above it as in cyclopia, and in Nicholson's there was pseudencephaly. In Barkow's case the only traces of a body were some rudimentary vertebræ and ribs.

The *acephalic* twin is sharply marked off from the paracephalic by the absence of a head; a trunk is usually present, but the fœtus may in some cases be reduced to a pelvis and lower limbs. This is the best known type of the allantoido-angiopagous twins; and it is relatively common, for Taruffi (*op. cit.*, ii. 174, 1882) was able to collect about 120 instances from literature, and there have been other instances described during the past twenty years. In the great majority of the records the heart is described as absent, so that the term "acardiac" has been used as synonymous with "acephalic"; but this is not an invariable rule, and a group has been constructed under the designation *acephalus thorus cardiacus* to include the rare exceptions. In these (*e.g.* in Wulfshein's specimen, *Diss. inaug.*, p. 13, Berolini, 1833) there is a trace of a structure which may be regarded as a heart. The more common variety, *acephalus thorus acardiacus*, has a thorax and occasionally some traces of upper limbs, but no heart; the arms, however, are often wanting as well as the heart. Again, the thorax may be absent and the fœtus reduced to an abdomen, a pelvis, and lower limbs; this type is known as *acephalus athorus*. Finally, just as the extreme limit of deformity in the paracephalians was reached in the presence of little more than a head, so in the acephalians it is attained in the existence of little more than the lower limbs (*acephalus pseudo-acormus*). A specimen somewhat difficult to classify was that reported by A. R. Simpson (*Trans. Edinb. Obstet. Soc.*, iii. 26, 1872); it showed *three* legs, and resembled the impression on an Isle of Man penny.

The *amorphous* twin is one which lacks the external appearances proper to a fœtus; it consists of little more than an ovate or rounded skin-covered mass with the indications of limbs (*fœtus amorphus mylacephalus*) or without these (*fœtus amorphus anideus*). The co-twin here, as in nearly all these varieties, is almost if not quite normally formed. I have seen two specimens of the mylacephalous twin; one was that reported to the Edinburgh Obstetrical Society by Sir Halliday Croom in 1893 (*Trans. Edinb. Obstet. Soc.*, xviii. 69, 1893), the other I had an opportunity of examining in the Obstetrical Museum in the University of Aberdeen in 1897. I have met with two cases of the anidean variety, one of which was described by J. C. Webster (*Teratologia*, ii. 178, 1895), and the other by myself (*Teratologia*, i. 1, 1894); the report of a third specimen, peculiar on account of the small size of the anidean fœtus (little over an inch in length), was sent to me by Drs. Ridley Mackenzie and John M'Crae of Montreal.

My specimen of anideus (Fig. 87) consisted of an ovate body about the size of the closed fist, completely enclosed in transparent membranes (chorion and amnion). Near one end, regarded provisionally as the upper, a few hairs were visible, and on one surface, regarded as the anterior, were certain elevations and grooves. An examination of the membranes showed that the fœtus was enclosed in an amnion of its own, and was also attached to the common chorion and to the amnion of the normal twin. In order to reveal the internal appearances a section was made through the mass (Fig. 88). There was an external covering of skin and a markedly œdematous subcutaneous substratum; below that was a dense layer of adipose tissue divided up into lobules by bands of connective tissue; under that again was an irregular layer of striped muscular fibres, showing a

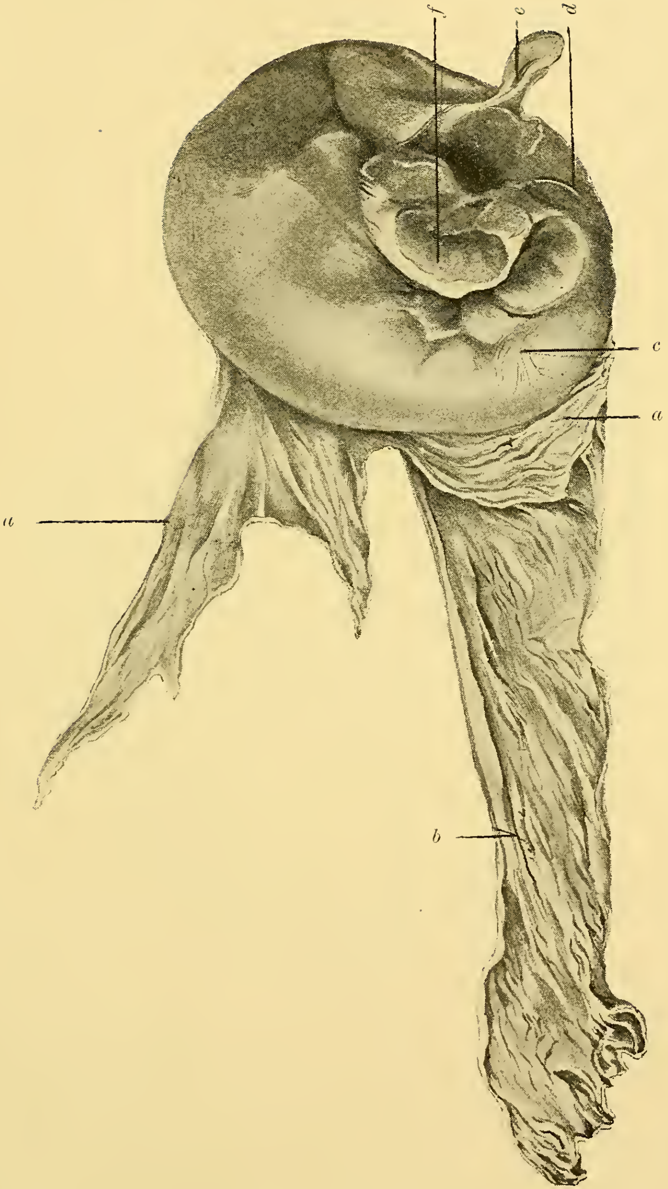


Fig. 87.—External Appearances of Fœtus Anideus and its Investing Membranes (reduced by about one-third).

a and *b*, amnion and chorion ; *c*, tuft of hairs near upper end ; *d*, blood vessel entering fœtus ; *e*, second blood vessel passing in tag of membrane ; *f*, projection on anterior aspect, containing coils of intestines.

kind of fatty degeneration, and lying in close contact with the osseous kernel. Here and there were sebaceous glands and blood vessels. On the anterior aspect, near the upper end of the fœtus anideus, was a furrow or fissure leading into a somewhat irregular cavity, lined by a smooth serous membrane and containing some loops of intestine (12 to 15 cms. in length). The osseous kernel consisted of a confused mass of pieces of bone and cartilage, which probably represented rudimentary sacral and coccygeal vertebræ. The vascular supply, an artery and a vein, passed to the fœtus in the membranes and entered it in the neighbourhood of the intestine-containing cavity.

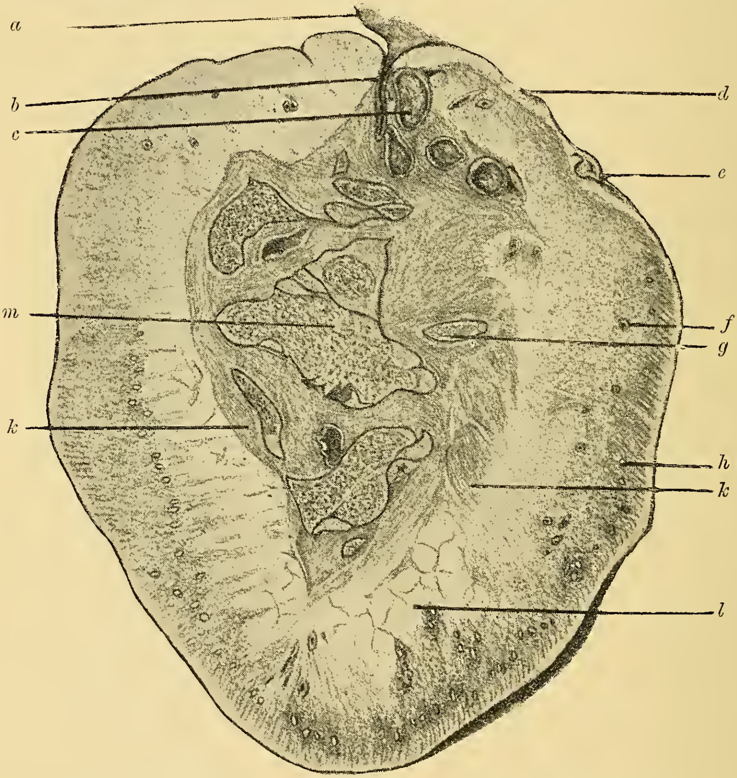


Fig. 88.—Sectional Appearances of Fœtus Anideus (natural size).

a, amnion passing into furrow; *b*, the furrow on anterior surface; *c*, coil of intestine; *d*, surface of large projection; *e*, slight furrow; *f*, blood vessels; *g*, long bone in transverse section; *h*, sebaceous gland; *k*, muscular fibres; *l*, adipose tissue; *m*, central osseous mass (vertebræ).

The *teratogenesis* of the allantoido-angiopagous twin has been the fruitful source of much speculation and of many ingenious theories. These strange twins have always excited interest and roused curiosity. At first they were used in arguments as to the method in which the fœtus was nourished, until it was discovered that the unborn infant receives its food supply through its umbilicus and not through its mouth. Then, again, the circulation of blood in them has been the subject of much discussion, for obviously the absence of a heart made it difficult to understand how that function could be carried on; at first the contractile force of the arteries was invoked, and then the heart of the normal twin was recognised as the propelling agent, and gradually the placental anastomoses were recognised and their significance realised. It came to be seen that the deformed twin was dependent upon the placental circulation of the normal co-twin for his life, such as it was, for, of course, there is no possibility of any other than an antenatal life for such grossly malformed fœtuses as the acephalic and the acormic.

Then a new series of difficult problems arose for solution. Why was one twin normal and the other so gravely malformed? How did the heart of one twin come to carry on the circulation of both? Many explanations were suggested, but they were unsatisfactory. Light began to be thrown on the subject when M. Claudius (*Die Entwicklung der herzlosen Missgeburten*, Kiel, 1859), F. Ahlfeld (*op. cit.*, p. 39, 1880), Dareste (*op. cit.*, 482, 1891), and F. Schatz (*op. cit.*, 1900) commenced to study it. The idea that one twin obtains a larger share of or an earlier attachment to the vessels of the chorion forms a good working hypothesis, and the details, although complicated, can then be elaborated and individual peculiarities explained. It may be that the allantois of one twin grows out earlier than that of the other; it may be that one twin's placental connection is through the omphalomesenteric vessels and not through the allantoic at all; in one way or another, one twin, as it were, becomes the predominant partner, and the other is so imperfectly nourished that it grows malformed and monstrous. If it were not for the twinship existing in the uterus no such malformed fœtus could be imagined to be capable of even an antenatal existence. One twin, then, according to this view, first starves the other, and, having reduced it to a markedly imperfect state, next keeps it alive by sending some of its blood to it through the placental circulation which is common to both. Another explanation, however, is possible: one twin may, to begin with, be imperfect, so imperfect as to be incapable of more than the most ephemeral antenatal life; but, through the presence of a twin embryo, it becomes attached to a new source of nourishment, and is, as it were, preserved in existence for a little longer time. According to the second explanation, the normal twin plays an entirely beneficent part; while, according to the first, it has a maleficent effect, and then, later, a beneficent one. It may be that the defective twin is one of those fractional individuals which experimental teratogeny has succeeded in producing, and that, but for the fact of the presence of a twin in utero, it would not have lived long enough to be recognised. The teratogenesis of the allantoido-angiopagous fœtus, therefore, resolves itself into two separate conditions, the twinship and the deformity; and it is not clear whether the former is the cause of the deformity or is the means by which the life of the deformed embryo is continued although but for a brief space of time. The whole question is one of the most interesting which can be well imagined.

United Twins or Double Terata.

If we imagine an allantoido-angiopagous twin situated so near to its normal co-twin as to be structurally continuous with it, we have one of the types of double monsters that we are now about to describe. For instance, a fœtus consisting of a trunk and limbs may be fixed to the epigastric region of a normal fœtus; this is just as if the umbilical cord attaching an acephalus to its co-twin had been shortened till it came to be unrepresented outside the body at all. Cases of this kind are called *asymmetrical* or *parasitic double terata*, and concerning them something more will be said immediately; but the more typical united twins are the *symmetrical* ones, those in which two individuals of practically the same size are more or less completely fused together.

To the first great type of the *symmetrically united twins* or *disomata* the name *syncephalus* has been given: in it the two fœtuses are joined together more or less closely by the heads, the trunks being either separate or fused. A synonymous expression is *prozygosis*. The chief sub-types, with their leading features, may be indicated in tabular form, Taruffi's arrangement being followed.

I. *Craniopagus:* Twins united solely by the heads.
  - *a.* Acrocephalus pagus. The union is by the sinciputs.
  - *b.* Iniopagus. The union is by the occiputs.
  - *c.* Metopagus. The union is by the frontal regions.

II. *Syncephalus thoracopagus:* Twins united by the heads and thoraces.
  - *a.* Diprosopus monopedius or Hemipagus. There are two faces more or less incomplete which are united laterally and are turned more or less from the abdominal aspect. The trunks are united as low as the umbilicus.
    1. Head with two faces and four eyes (diprosopus tetraophthalmus).
    2. Head with two faces and three eyes (diprosopus triophthalmus).
    3. Head with rather wide face (really two) but only two eyes (diprosopus diophthalmus).
  - *b.* Janiceps teleus. There are two more or less perfect faces, placed opposite to each other and symmetrical.
  - *c.* Janiceps ateleus. One of the two opposite faces is imperfect, *e.g.* has a median eye (Janiceps cyclopus) or two rudimentary approximated ears (Janiceps synotus).
  - *d.* Syncephalus monoprosopus. There is a single head and face with two thoraces and the trunks are separate below the umbilicus.

III. *Syncephalus dilecanus:* Twins united so that there is a single head and thorax but two more or less complete pelves. Synonyms, s. ileopagus or ileadelphus.
  - *a.* Dilecanus dipleurus. The two pelves are inserted laterally upon a vertebral column which shows signs of duplicity posteriorly.
    1. There are four lower limbs (Dilecanus dipleurus tetrapus).

2. There are two lower limbs but two penes or vulvæ, and signs of duplicity in sacrum (Dilecanus dipleurus dipus).

b. Dilecanus ibipagus. The ilia of one pelvis are fused with those of the other by means of the pubic bones, so that there is a single pelvic cavity.

1. Each pelvis has its ilia complete with their acetabula (Dilecanus ibipagus tetrapus).
2. Each pelvis has only the external ilium complete, the internal ilia being incomplete and having only one acetabulum for both (Dilecanus ibipagus tripus).

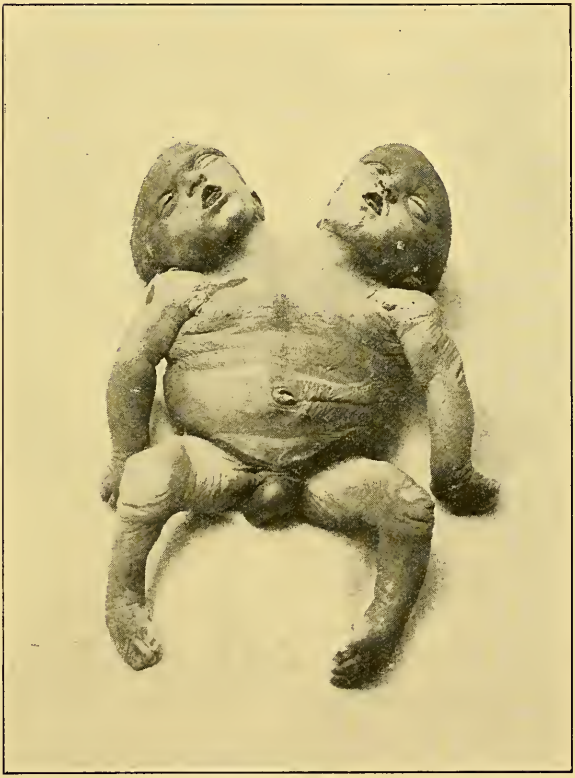


Fig. 89.—Dr. Pallarés' Dicephalic Twin Fœtus, Variety Dipus Dibrachius.

These, then, are the various sub-types of the syncephalic double monsters. Perhaps the best known and most striking of them are the Janus or double-faced twins, some good examples of which are in the Museum of the Royal College of Surgeons of England (Thompson Lowne's *Descriptive Catalogue*, p. 29, 1893). The curious cases of twins united only by the vertices (craniopagus) are very rare, and seem to have been more often reported in Russia than any other country. It will be noted that some of these sub-types, *e.g.* the cases of double penis (Dilecanus dipus diphallus), can hardly be separated from the monosomatous terata, among which, indeed, I have described them (p. 554).

To the second great type of the symmetrically united twins the names of *dicephalus* and *lecanopagus* have been given. These monstrosities show a more or less intimate union of the pelves and the parts below, along with a separateness of the heads and usually also of the necks and of part of the thoraces. I give illustrations of two of the chief sub-types (to be enumerated below): one (Fig. 89) represents a specimen in the possession of Dr. Pallarés of Lorca in Spain (to whom I am indebted for the photograph), which showed two separate heads and necks, a common trunk, containing (as was found on dissection) a double respiratory apparatus and a single heart and digestive system, two arms and two legs, and a single penis and scrotum. Its birth was complicated with placenta prævia, and it was extracted dead (*Teratologia,* ii. 210, 1895). It belonged to the group of dicephalus dipus dibrachius. The other illustration (Fig. 90) is also taken from a photograph, and it formed one of a series kindly sent to me by Dr. Michin of Charkow in Russia. It belonged to the variety dicephalus tripus tribrachius. Each fœtus had a heart and lungs; the two hearts lay in one pericardium; there was one sternum for the two; there was only one clavicle but two scapulæ for each. In the fused upper limb there was one humerus, but two ulnar and two radial bones were present. The vertebral columns were separate above but united below in a single sacrum. There was a single liver, spleen, and intestinal canal for the two fœtuses. The pelvis was split anteriorly (pelvis fissa), there was ectopia vesicæ urinariæ, and the penis and scrotum were double, there being one testicle in each scrotum. On the posterior aspect of the sacral region was a third imperfectly developed lower limb, which had no femur, but only the bones of the leg and one large digit. The chief varieties of dicephalic united twins are as follow :—

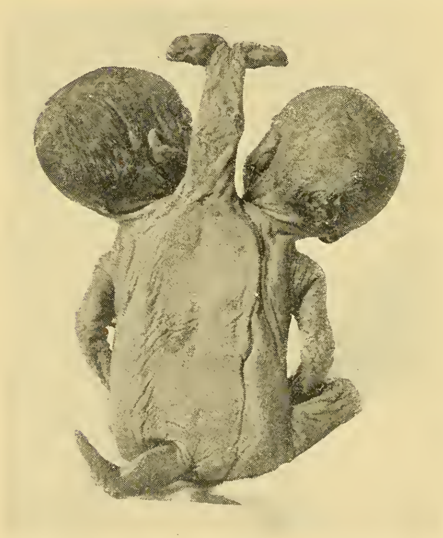


FIG. 90.—Dr. Michin's Dicephalic Twin Fœtus, Variety Tripus Tribrachius.

I. *Lecanopagus tetrabrachius et tetrapus:* Twins united by the pelves, each having its own limbs.
    a. Ischiopagus. The union is by the innominate bones, a single pelvic cavity resulting.

- *b.* Pygopagus. The union is by the region of the nates, each twin having its own pelvis, directed outwards.

II. *Lecano-Somatopagus:* Twins united by the pelves and thoraces or through the spinal columns directly.

- *a.* Somatopagus parallelus. The twins have their axes parallel, and are united by the pelves and thoraces; there are four legs and arms.
- *b.* Somato-catagoniodes tripus. The union is by the pelves and thoraces, and there are three legs; there may be four arms (tetrabrachius) or three (tribrachius).
- *c.* Somato-catagoniodes dipus. The union is by the pelves and thoraces, and there are two legs; there may be four (tetrabrachius), three (tribrachius), or two (dibrachius) arms.
- *d.* Somato-mesopagus. The union is by the middle parts of the axes; there is separation above and below.

III. *Lecanopagus Diprosopus:* Twins united by the pelves and thoraces, and having also the heads joined together laterally.

- *a.* Diprosopus tetraophthalmus or Iniodymus. There is a single body with two heads joined laterally and converging so as to describe an angle with its apex inferior; each face has two orbits.
- *b.* Diprosopus triophthalmus. There is a single body with two heads fused together laterally and converging so as to form an angle above, leaving space for only three eyes.
- *c.* Diprosopus diophthalmus. There is a single body with a head larger than usual, with two eyes, two noses, and one or two mouths.

In the dicephalic twin fœtuses, just as in the syncephalic, the terminal members of the series tend to approximate closely to the monosomatous terata, and to become difficult of separation. A good example of this is seen in Diprosopus diophthalmus, in which the size of the head and the presence of two noses may be almost the only signs of duplicity. I must find space here for a few words of description of a well-known historical instance of dicephalus, the "Scottish Brothers," who lived in the reign of James IV. of Scotland, and about whom Lindesay of Pitscottie wrote in his inimitable fashion. "In this mean Time there was a great Marvel seen in Scotland. A Bairn was born reckoned to be a Man-Child; but, from the Waste up, was two fair Persons, with all Members and Portraitures pertaining to two Bodies, to wit, Two Heads, well-eyed, well-eared, and well-handed. The two Bodies, the One's Back was fast to the Other's; but, from the Waste down, they were but one Personage, and could not know by the Ingyne of Man, from which of the two Bodies the Legs and Privy Members proceeded. Notwithstanding the King's Majesty caused take great Care and Diligence upon the Upbringing of their two Bodies in one Personage, caused nourish them, and learn them to sing and play upon Instruments of Musick; who, within short Time, became very ingenious and cunning in the Art of Musick; whereby they could sing and play two Parts; the one the Treble, and the other the Tenor; which was very dulce and melodious to hear. The common People who treated them also, wondered that they could speak diverse and sundry Languages: that is to say, Latin, French, Italian, Spanish, Dutch. Danish, English, and Irish. Their two Bodies long continued, to the age of twenty-eight years: and the one departed long before the other, which was dolorous and heavy to the other; for which many required of the other to be merry. He answered. How can I be merry, that have my true Marrow as a dead Carrion about my Back, which was wont to sing and play with me. When I was sad he would give me Comfort, and I would do the like to him: But now I have nothing but Dolour of the Bearing so heavy a Burden, dead. cold, and unsavoury, on my Back, which taketh all earthly Pleasure from me in this present Life: Therefore I pray to Almighty God, to deliver me out of this present Life, that we may be laid and dissolved in the Earth, wherefrom we came."

The third and last of the great subdivisions of the symmetrically united disomata contains the well-known and comparatively common *thoracopagous monsters* (*emprosthozygosis*, Thompson Lowne). They are twins joined together by the epigastric regions and by more or less extensive parts of the thoraces. To them belong such historical instances as the Siamese twin-brothers, Maria-Rosalina, operated on by Chapot-Prévost of Rio de Janeiro (*Chirurgie des teratopages*, Paris, 1901), and the Radica-Doodica sisters, separated by Doyen. I have met with a specimen of this type (Fig. 91), and, recently, R. J. A. Berry described very fully two other cases (*Trans. Edinb. Obstet. Soc.*, xxviii. 220, 1903). There are altogether many instances of thoracopagous twins on record, and the literature is to be found in Taruffi's work (*op. cit.*, ii. 515, 1882: iii. 507, 1885; iv. 224, 1886; viii. 458, 1894) and the *Index Catalogue* (vol. ix. 394, 1888; xiii. 1, 1892). The sub-types are as follow:—

I. *Xiphopagus:* Twins united by the epigastric regions and by the ensiform cartilages of the sterna.
II. *Sternopagus:* Twins united by the sterna and by the epigastric regions, and separate in all the other parts.
  a. Sternopagus tetrabrachius. Each twin has two upper limbs (Fig. 91); the internal organs, and more particularly the heart, show various degrees of fusion.
  b. Sternopagus tribrachius or ectopagus. The twins are rotated somewhat outwards; there are three arms, one being median and posterior.
  c. Sternopagus dibrachius. The twins are rotated markedly outwards and each has one upper limb.

If sternopagous twins can be extracted alive from the uterus, they not uncommonly survive their birth, but most frequently one or both of the fœtuses has to be broken up before delivery can be accomplished. With modern surgical asepsis renewed efforts have, of recent years, been made to separate such united twins, more especially when one of them became the subject of such a disease as tuberculosis. Thus far, the results have been encouraging, but not brilliantly so. Skiagraphy will doubtless enable the surgeons of the future more carefully to choose the proper cases for operation, and with better means of checking hæmorrhage (*e.g.* from the liver) he will almost certainly be able to separate twins of the xiphopagous type at any rate.

The *asymmetrically united twins* or *parasitic double terata* are not so easily classified as are the symmetrical ones. At the one end of a long series of types is the fœtus (or autosite) with an attached fœtus (or parasite) defective in some part, but not much smaller than the autosite; at the other end of this series are such conditions as the fœtus in fœtu (or included twin) and dermoid cysts, teratomata, and, perhaps, polydactyly and polymastia. This, like so many other parts of the classification of teratological states, shades off in an indefinite manner into neighbouring or allied types: fœtus in fœtu passes by degrees into tumours of various kinds, and polydactyly is not far removed from the single (monosomatous) terata if, indeed, it be not included in them. Perhaps the best arrangement that we can adopt for these defective, attached, or included fœtuses is the regional; we discuss, therefore, the parasites of the head, face, neck, thorax,

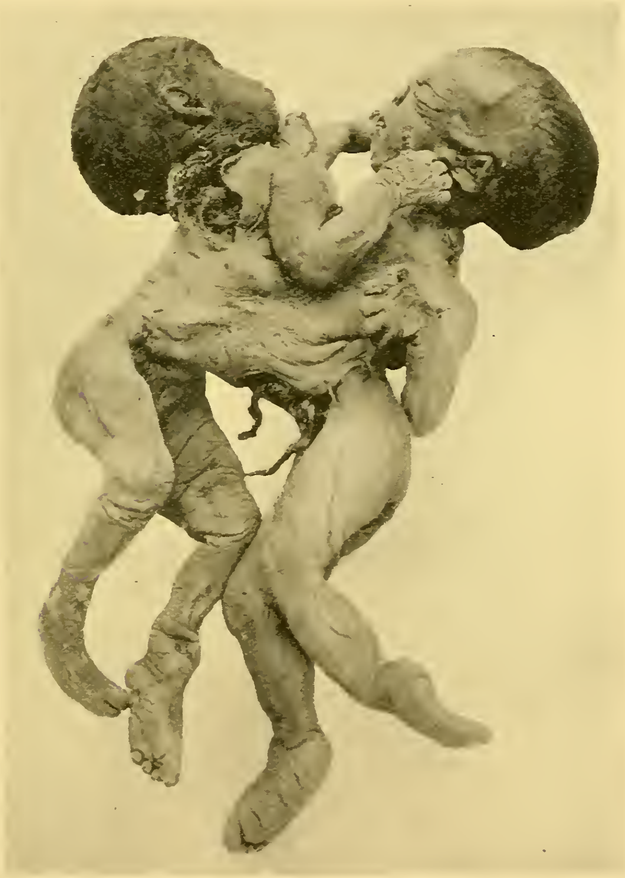


FIG. 91.—Thoracopagous Twins.

abdomen, pelvis, and limbs. A few words must suffice about each in turn.

I. *Cephalo-Parasitus.*—This group includes the epicoma or cephalo-paracephalus, the fœtus with limbs and sometimes with a defective body which is attached by its sinciput to that of the perfect twin; there are sub-varieties (dipus, apus, and pseudo-acormus) according as the parasite is provided with limbs or not. It also includes the cephalo-diprosopus, in which the autosite carries on the side or front of its head a second more or less incomplete head; the cephalomeles, in which an accessory limb is inserted on the head; the encephalo-amorphus, in which a tumour, with fœtal parts, is inclosed within the cranium; the teratoid intra- or extra-cranial growth; and the dermoid cysts, situated inside or outside the cranium.

II. *Trachelo-Parasitus.*—This group contains a number of parasitic growths of the neck and lower part of the face. It includes such cases as that of accessory superior maxilla attached to the superior maxilla of the autosite, of which the specimen shown in Figs. 70 and 71 was probably an example. It includes also the accessory parts attached to the lower jaw; and here may be placed the instances of a supernumerary limb arising from the neck, which have as yet only been met with (and that rarely) in animals (aucheno-melus or dero-melus); here also the extraordinary state known as epignathus, in which a tumour containing fœtal parts springs from the palate and protrudes through the mouth, may find its proper position in a system of classification. Some of the cervical cysts, teratoid or dermoid in character, must likewise be included here, and perhaps also the instances of cervical auricles (pleonotus).

III. *Thoraco-Parasitus.*—Individuals like the Chinaman Aké and the boy Laloo, in which a nearly complete but small fœtus is attached to the anterior aspect of the thorax, belong to this group. Sometimes the parasite may have a rudimentary head (thoraco-paracephalus or heteropagus), sometimes it has little more than a head (thoraco-paracephalus pseudo-acormus or heterodymus), but most often it has no head at all (thoraco-acephalus or heteradelphus). In another group of cases accessory limbs spring from the thorax (thoraco-melus), either from the posterior aspect (notomelus) or from the side (pleuro-melus). Teratoid and dermoid growths may also be found attached to or lying inside the thorax; and, finally, the rigid laws of classification (which are not represented in Nature) would place polymastia or accessory mammary glands here.

IV. *Gastro-Parasitus.*—It is comparatively rare to find an acephalic fœtus (gastro-acephalus) or a supernumerary limb (gastro-melus) attached to the abdomen of the autosite; but the curious included embryos (gastro-amorphus), the cases of fœtus in fœtu or congenital pregnancy, are not so very rare. I gave an account (*Brit. Med. Journ.*, ii. for 1900, p. 1428) of the dissection of one of these remarkable amorphous fœtuses which was removed by Mr. Wright of Manchester from the cavity of the lesser peritoneum of a female child aged two months. Its appearances are shown in Figs. 92 and 93; and its structure closely resembled that of the twin fœtus amorphus anideus already described (p. 628). In this group, also, must be placed the teratomata of the scrotum, and the teratoids and dermoid tumours of the abdomen, the testicle, and the ovary.

V. *Lecano-Parasitus.*—Parasitic attachments to the pelvis and neighbouring parts are very difficult to classify or to understand. They include the sacral and perineal teratomata, an example of which I saw in December 1903 under Mr. Stiles' care in the Edinburgh Sick Children's Hospital. Perhaps the best idea of the various parasitic growths found in this region of the body may be obtained from the consideration of Taruffi's classification (*op. cit.*, iii. 316 *et seq.*, 1885).

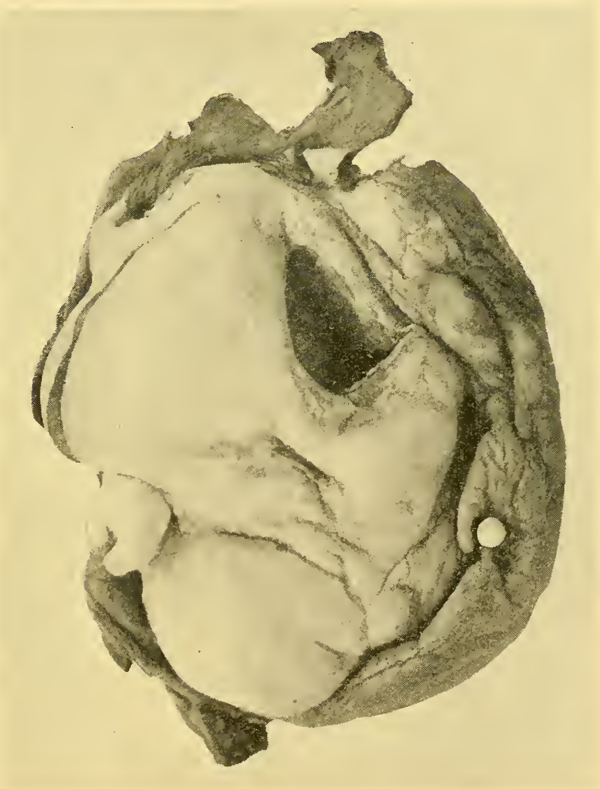


Fig. 92.—Appearances of Dermal Aspect of Fœtus in Fœtu.

a. *Ischio-parasitus.*—The parasite is attached to the ramus of the pubes or to the perineum of the autosite; and it may consist of an acephalus or a paracephalus (heteromorphus and heterotypus of Saint-Hilaire's nomenclature), or of an amorphus, or simply of an accessory limb (ischio-melus) as in the well-known case of the man Dos Santos (the "human tripod").

b. *Ilio-parasitus.*—The parasite consists of one or two accessory limbs attached to one or both iliac bones; it is a very rare state in the human subject, but less rare in animals.

c. *Ischio-sacro-parasitus.*—This group contains the parasitic fœtuses (generally of the nature of accessory limbs) which are attached to the ischia and sacrum and spring from the sciatic notch.

d. *Pygo-parasitus.*—Here are included the accessory limbs adhering to the nates (pygomelus); the sacral teratomata (pygo-amorphus), in which the attachment is not so much to the sacrum as to the parts covering it; the teratoid growth of the nates (pygo-teratoides); and the dermoid cysts of the same region.

VI. *Melomelus.*—This group includes the cases in which an accessory limb or part of one is inserted upon another normal limb.

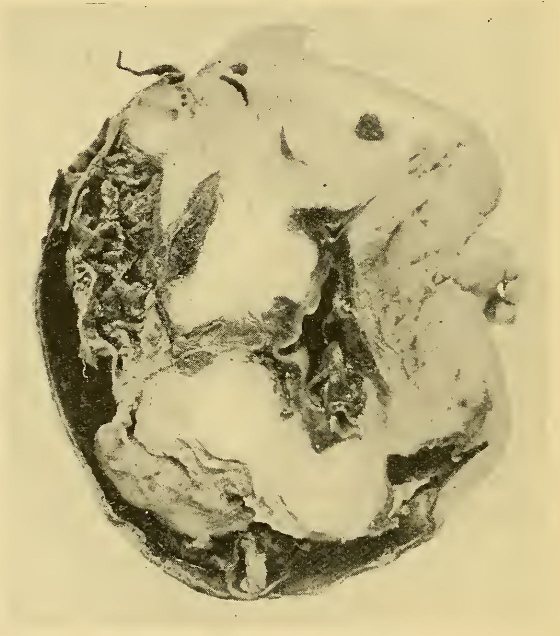


FIG. 93.—Section of Fœtus in Fœtu, showing much adipose tissue, pieces of cartilage, and cavities lined with pigmented membrane.

It is the most artificial of the groups into which the asymmetrically united double terata have been divided. Cases in which a supernumerary limb is attached to the normal femur or humerus are rare, but authentic instances have been observed; the insertion of an accessory member upon the bones of the leg or of the forearm has not been observed in the human subject; but there have been a few examples of double hand (dichirus) and double foot (dipus), and to these reference has already been made under the monosomatous terata. Perhaps the most artificial and strained part of the whole of this system of teratological classification is the inclusion of polydactyly here among the double terata. Although, theoretically, it may be correct, I have not hesitated for once to abandon the classificational system for common sense, and accordingly I dealt with polydactyly along with the malformations of the limbs. This concludes the long list of the types of the polysomatous terata, diæretic as well as synæretic.

I have endeavoured, in the preceding pages, to give an idea of the scope of the subject of double monsters ("diplo-teratology") and to refer, shortly at least, to most of the leading types. It will have been noticed that almost every imaginable combination of characters has been enumerated: the twins have been attached by the heads, by the backs, by the chests, by the pelves, and so on; and, generally speaking, the rule of "like parts being attached to like" has been observed. Among all the wealth of observation and the multiplicity of forms there are still some lacunæ in our knowledge which time may perhaps fill up. Every double monster is well worth dissecting.

I may refer, here, in passing to one of the most interesting of the double terata, the historical instance of the "Biddenden Maids." These were maidens, supposed to have been born in the year 1100 in the village of Biddenden in Kent, who lived joined together for thirty-four years, and at their death left money to be employed in the baking of cakes or rolls with their impression on them which were to be distributed to the poor every Easter Sunday. I collected sometime ago all the details of their history that I could find (*Teratologia*, ii. 268, 1895), and the representation of them, as it appears on the cakes and broadside, is reproduced in Figs. 94 and 95. The reason why I refer to them at all is twofold: first, because they are the earliest known English double terata, and, second, because their mode of union, if correctly represented, is unique. It would appear from Fig. 95, but more especially from Fig. 94, as if the maids were joined by the arms at the elbows. Now it is unwise to say that any particular mode of union of double terata is impossible; but it seems to me probable that in this respect the artist took a liberty with the facts. Probably the maids were pygopagous twins like the well-known

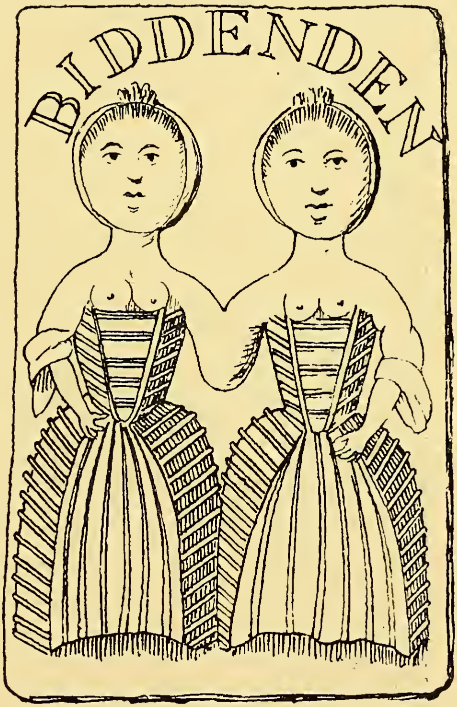
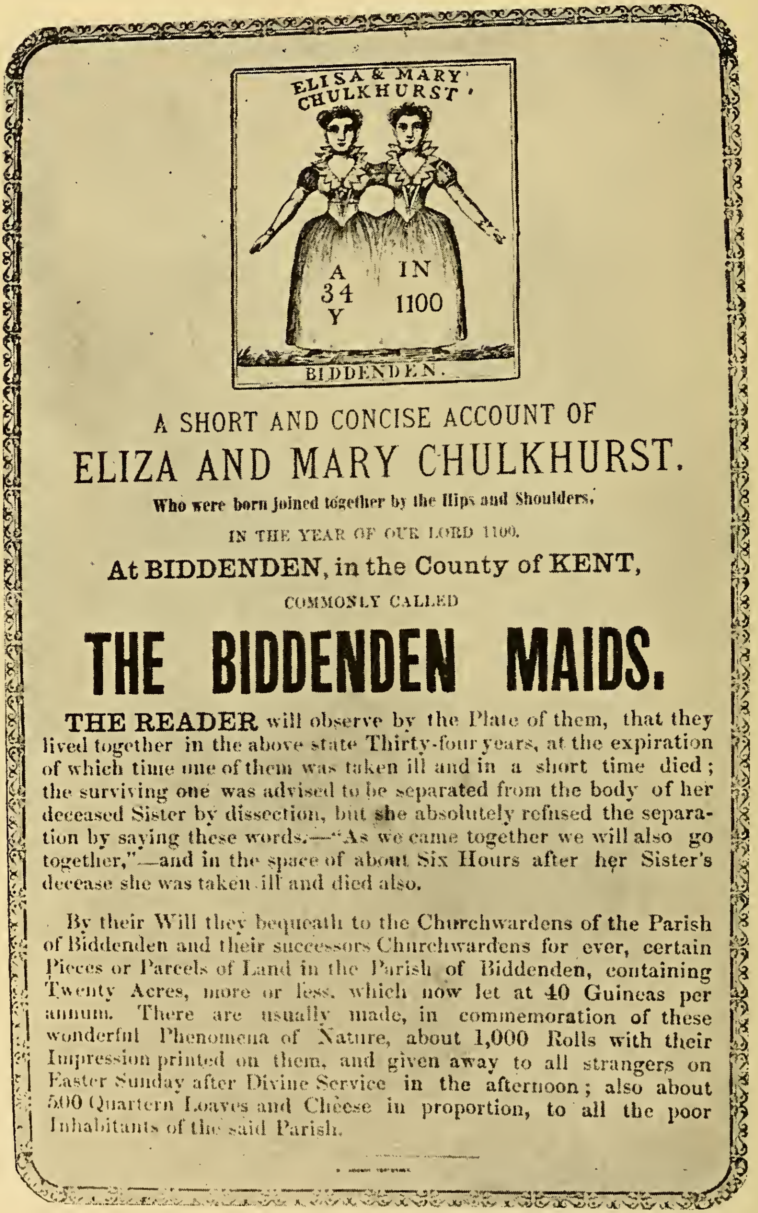


Fig. 94.—The Biddenden Maids.

Hungarian sisters (Helen and Judith), the North Carolina twins (Millie and Christine), and the Bohemian twins (Rosalie and Josepha


ELISA & MARY CHULKHURST
A 34 Y
IN 1100
BIDDENDEN.

A SHORT AND CONCISE ACCOUNT OF

ELIZA AND MARY CHULKHURST.

Who were born joined together by the Hips and Shoulders,

IN THE YEAR OF OUR LORD 1100.

At BIDDENDEN, in the County of KENT,

COMMONLY CALLED

THE BIDDENDEN MAIDS.

THE READER will observe by the Plate of them, that they lived together in the above state Thirty-four years, at the expiration of which time one of them was taken ill and in a short time died; the surviving one was advised to be separated from the body of her deceased Sister by dissection, but she absolutely refused the separation by saying these words.—"As we came together we will also go together,"—and in the space of about Six Hours after her Sister's decease she was taken ill and died also.

By their Will they bequeath to the Churchwardens of the Parish of Biddenden and their successors Churchwardens for ever, certain Pieces or Parcels of Land in the Parish of Biddenden, containing Twenty Acres, more or less, which now let at 40 Guineas per annum. There are usually made, in commemoration of these wonderful Phenomena of Nature, about 1,000 Rolls with their Impression printed on them, and given away to all strangers on Easter Sunday after Divine Service in the afternoon; also about 500 Quartern Loaves and Cheese in proportion, to all the poor Inhabitants of the said Parish.

Fig. 95.—"Broadside" of the Biddenden Maids.

Blazek). They were, doubtless, united by the nates in a postero-lateral manner, and the idea of union by the arms may have arisen from their going about with their arms round each other's necks.

The *teratogenesis* of the united twins has, as might well be imagined, excited much interest and discussion. I have no space to enter into the long controversy, not yet finished, concerning the origin of the various types of double terata; but I may say that I am inclined to accept the theory of polyspermy as the determining cause of these monstrosities, although possibly in some cases, more especially in relation to the parasitic or included fœtuses, the notion of parthenogenetic development in an ovum or in the testicle may be entertained. We may suppose that the entrance of one spermatozoon into the ovum determines the appearance at a later date of one embryonic rudiment with a definite orientation in the blastocyst; if, now, two fertilising spermatozoa gain entrance, two primitive streaks, each with its own orientation, may be looked for; according to the proximity or separation of the primitive streaks will be the relation of the future twins. The streaks may be in opposition to each other, when the craniopagous type of double monster may result; they may lie side by side, when thoracopagous twins will be produced; or they may be inclined towards each other either at their anterior or posterior ends, when syncephalic or dicephalic terata will be formed. A still closer union of the primitive streaks may suffice to explain the parasitic types. It must always be borne in mind, also, that in considering included fœtuses there is a time in development when the body cavity of the embryo is not closed and when it is quite possible for one rudimentary embryo to become surrounded by the other and the larger twin ("enclavement"). In all these monstrosities the twinship is, to my mind, the essential and original pathological fact. The reader, who desires it, will find a suggestive account of the origin of double terata in Duval's article, in Bouchard's *Traité de pathologie générale*, i. pp. 211–233, 1895.

Triplets and Quadruplets, etc.

Pregnancies with more than two children, whether they be monochorionic or dichorionic, must be regarded as teratological. A few sentences must be devoted to triplets and a few words to the rarer quadruplets and quintuplets.

Triplets occur about once in seven thousand pregnancies. They are, however, much more likely to occur in the case of women who have given birth to twins or are the mothers of large families; a woman, herself a twin, has been known to give birth to triplets. Uniovular triplets do not appear to be hereditary, while binovular and triovular ones often are. All the morbid states of pregnancy (*e.g.* albuminuria, œdema, hæmorrhage) are more frequent in triplet gestations; vertex presentations diminish in frequency and abnormal ones (breech and shoulder) increase. About 50 per cent. of the infants are to be regarded as viable, but only about 33 per cent. survive the first year of life. They are most often of different sexes (two boys and one girl, or two girls and one boy), but it is not uncommon to find them all of one sex (three boys or three girls). When we come to study the membranes, we find that triplets may be triovular (three chorions and three placentas or more often two placentas), or binovular (two chorions and two or rarely one placenta), or uniovular (one chorion and one placenta). The binovular are the commonest and the uniovular the rarest types; in 1901, R. Saniter (*Ztschr. f. Geburtsh. u. Gynäk.*, xlvi. 347, 1901) was only able to collect together records of eight well-established cases of uniovular triplets, and although Walla (*Centrlbl. f. Gynäk.*, xxvi. 403, 1902) has reported another, they are undoubtedly very rare. The amniotic sacs seem always to have been separate.

One of the triplets is not uncommonly an acardiac; curiously enough, the recorded instances have so far been all but one in the binovular variety; in other words, they have been cases of allantoido-angiopagous twins born along with a third fœtus. The single exception is that reported by G. Giglio (*Arch. di ostet.*, iii. 235, 1896); in it there was a single chorion and three distinct amnions, one of which showed hydramnios and contained an acephalic embryo. An instance of uniovular triplets, one of which was a fœtus papyraceus, was reported by von Erlach (*Centrlbl. f. Gynäk.*, xviii. 439, 1894); a case of triplets, two of which were fœtuses papyracei and one was a living child, was described by C. Gutmann (*Diss. inaug.*, Strassburg, 1885). *United triplets* or *triple terata* are so rare as to be almost unknown. A case of a tricephalic infant was reported in the year 1834; it consisted of three heads set upon two united trunks, supported by two lower limbs; there were three upper limbs and a single set of male genitals; all the heads had to be perforated during labour, and two of them amputated. The occurrence was reported by Reina and Galvagni (Saint-Hilaire, *op. cit.*, iii. 341, 1836). Perhaps the most extraordinary monstrosity ever put upon record was that described by J. Baart de la Faille in 1874 (*Iets over den Epignathus*, Groningen): it consisted of a female fœtus, from whose mouth protruded a large tumour (epignathus), and to this tumour were attached by their umbilical cords two small acephalic fœtuses, each consisting of only the pelvis and two lower limbs. If we regard the epignathus as part of the autosite, this was a case of two parasitic fœtuses inserted upon it by their cords; but if we regard the epignathus as itself a parasite attached to the autosite, then we are in view of a teratological complex which could hardly have been imagined had the specimen not existed.

I must bring these notes on triplets to a conclusion with a reference to the curious case reported by G. W. Thompson (*Indiana Med. Journ.*, p. 373, April 1899): united twins of the female sex with two heads, four arms, four legs, and two bodies united by the thoraces, were expelled at the seventh month of pregnancy and breathed for twelve minutes; they were preceded, however, by the birth of a single male infant, which had a separate placenta and membranes.

The bibliography of triplets and triple monsters will be found in the *Index Catalogue* (vols. ix. 405, 1888; xiv. 775, 1893), and in R. Saniter's article (*Ztschr. f. Geburtsh. u. Gynäk.*, xlvi. 347, 1901).

Quadruplets are still rarer than triplets, occurring perhaps about once in 370,000 labours. At the same time, over seventy cases have been recorded in medical literature (*Index Catalogue*, xi. 919, 1890). Theoretically they may be derived from one, two, three, or four ova, and may be normal, deformed, or united together by their cords or structurally; but they are not numerous enough to allow of generalisations being made. A similar statement may be made regarding the state of their placentæ and membranes.

With regard to the occurrence of an allantoido-angiopagous fœtus as one of quadruplets, I may refer to Dr. Günsburg's extraordinary observation, communicated by me to the Edinburgh Obstetrical Society in 1896 (*Trans. Edinb. Obstet. Soc.*, xxi. 250, 1895–96). The mother, a Russian peasant woman, aborted at the fourth month of her first pregnancy of four separate fœtuses, one of which was monstrous (paracephalic). Three were males (including the paracephalus) and one was a female; there were two separate placental masses, one of which was made up of three placentas united into one, and the other was single. It was then a case of uniovular triplets with a single fœtus; it was a binovular pregnancy in which one of the ovules produced three male fœtuses and the other a single female fœtus.

Charbonnier (*Étude des grossesses triples et plus que triples*, p. 65, 1895) refers to one or two cases of double terata born with two other fœtuses, and J. M. Rodriguez (*Gac. méd. de Mexico*, v. 17, 33, 1870) described a quadruple human monster; but exact records are very rare, and I have not been able to consult either the case of Rodriguez or those mentioned by Charbonnier in the original.

Recent instances of quadruplets have been recorded by Stahl (*Trans. Chicago Gyn. Soc.*, p. 6, 1896), C. C. Henry (*Brooklyn Med. Journ.*, x. 618, 1896), Bousquet (*Ann. de gynéc.*, xlii. p. 55, 1894), Schatz (*Kor.-Bl. d. allg. mecklenb. Aerztever.*, No. 190, p. 568, 1898), E. T. Goode (*Lancet*, i. for 1897, p. 590), and O. Ausch (*München. med. Wchnschr.*, xxii. 123, 137, 1897).

Quintuplets are among the curiosities of obstetrics, occurring as they do not oftener than once in many millions of labours (1 in 13,400,000, Charbonnier). In the *Index Catalogue* (xi. 968, 1890) there are references to twenty-one cases; recently a few more cases have been added, including those of R. A. Hibbs (*Amer. Med. Surg. Bull.*, x. 267, 1896), of Stoker (*Lancet*, ii. for 1895, p. 1164), and of Sato (*Sei-i-kwai Med. Journ.*, xxi. 40, 1902). In Sato's case there were three placental masses, two with two cords each, and one with one; the infants were three males and two females; in Stoker's, the placenta consisted of two parts united by an isthmus, and one part had two and the other three cords attached to it; while in Hibbs' case there were five cords attached to one placenta. G. C. Nijhoff's quintuplets (*Nederl. Tijdschr. v. Geneesk.*, ii. for 1903, p. 1305; *Journ. Obst. Gynæc. Brit. Empire*, vi. 32, 1904) were four females and one male, and were born alive, but, being immature, survived only one hour. The placenta consisted of one continuous cake, to which five separate cords were attached; each fœtus had its own amnion, but three had a common chorion and the two others a separate chorion; the case was, therefore, a triovular one. On the mother's side there were several instances of multiple pregnancy: her mother once had twins; two maternal uncles became fathers of twins; and a maternal aunt was delivered of triplets. Little is known concerning monstrosities in quintuplets; but in F. Poljakoff's case (*Med. Obozr.*, xxiii. 1015, 1885) one of the fœtuses was a microcephalus.

Sextuplets have been reported on a few occasions, but the records have usually been received with doubt. At any rate the reporters of the cases have seldom been actually present at the confinement. In this respect the recent instance of Drs. Kerr and Cookman (*Med. Press*, lxxv. 537, 1903) does not differ from the usual rule. The mother, a woman of the Gold Coast, was found lying exhausted in a hut, and six fœtuses were found beside her. The infants were five boys and one girl; there were four placentas, of which one belonged to the girl, one to one of the five boys, and the other two to two boys each. It was said that labour had lasted only four hours, and that each placenta was born after the children to whom it belonged. This was the woman's fourth pregnancy; in her first she had given birth to quadruplets, and in her second and third ones to triplets in each instance. There had thus been the extraordinary record of sixteen children in four pregnancies.

Other instances of sextuplets have been referred to by Guzzoni degli Ancarani (*Rassengna di sc. med.*, Modena, iv. 437, 489, 569, 617, 1889) and F. Vassalli (*Gazz. med. ital. lomb.*, xlviii. 216, 1888; *Ann. di ostet.*, xvi. 343, 1894).

Sextuplets in the human subject are of doubtful authenticity, but cases of *septuplets* are almost mythical. There is a story (Charbonnier, *op. cit.*, p. 83) of a man so alarmed by the rapid growth of his family that he left his home for seven years; a year after his return his wife gave birth to seven infants! Charbonnier also refers to two or three other reported cases; Roy (*Rév. med. franç. et étrang.*, i. 255, 1877) also dealt with the subject; and I may conclude with the following quotation from J. B. Bianchi (*De Naturali in Humano Corpore, Vitiosa Morbosaque Generatione*, p. 249, 1741): "Sic nostrâ hac ætate, nostrâque in hac Urbe, tres eodem partu, semel iterumque sunt editi: In quibusdam Pedemontanis Regionibus interdum quinque: et in Insubriæ Pago non diu ab hinc, septem simul in lucem prodiere. Namque non ita pridem testatus est mihi, R. P. David, Clericus Regularis Theatinus piissimus, nostrique Academici Sacelli Præfectus; ante hos annos xiv progredientem se Mediolano Robeccum, ad navigabilem Canalem habuisse obviam Mulierem, sibi jam famâ notam, quæ uno partu septem filios, masculos feminasque, vivos et vitales omnes, cito quidem, at non sine magnis cruciatibus, pepererat; tum vero ex iis primum aut alterum, masculumque, obviæ ipsius Matris vidisse comitem; cujus tum ætas xi aut xii annorum esse potuisset."

CHAPTER XXXIII

Pathology of Germinal Life (*cont.*): Physiology of the Egg- and Sperm-Cell; Normal or Ancestral Heredity; Pathology of the Egg- and Sperm-Cell; Popular and Scientific Ideas regarding Morbid Heredity and its Various Phenomena; Degeneration; Effect of Impregnation upon Heredity and Degeneration; Arrest of Growth, Development, and the Performance of Functions; Etiological Uniformity in the Various Periods of Life; Treatment of Antenatal Morbid States, and especially of those arising in the Germinal Epoch.

I ENTER with reluctance upon the discussion of the effect of morbid influences upon antenatal life still in the ovular and sperminal stage; I hesitate to attempt even to outline my views, or rather my view of others' views upon it. But having gone thus far in my search after the causes of antenatal disease, deformity, and malformation, I can hardly refuse to pass on a step or two further, even although it be in almost complete darkness that the advance is made. At the same time the reader must not imagine that I am now for the first time referring to the influence of morbid agents upon the egg-cell and sperm-cell before their fusion in fertilisation; both in this volume and in the one which preceded it I have already dealt incidentally with morbid heredity, for that is but another name for the pathology of the ovum and spermatozoon. I have referred to it more particularly when considering the transmission of syphilis from parent to child (Vol. I. p. 251), and have alluded to it when writing of the hereditary nature of certain malformations (polydactyly, hare-lip, etc.). Morbid heredity has really been with me in the writing of each chapter, and upon it I have not infrequently fallen back when faced by exceedingly difficult problems in teratogenesis. But it is a subject about which so very little is known and concerning which so very, very much has been spoken and written, that the seeker after truth is bewildered and rendered well-nigh hopeless. It is being crushed beneath a ponderous load of theories, many of them contradictory, and all of them built up upon scanty data. Is it matter for surprise if I approach with great reluctance the study of a subject upon which I can hardly hope to throw much light, while I may justly fear that I may very easily increase the existing darkness? The matter, however, must be dealt with if this MANUAL OF ANTENATAL PATHOLOGY is not to be left with one very important factor in antenatal morbid processes omitted. I can at least endeavour to earn for my presentation of the subject the merit of brevity; and if anything that appears here lead the reader to the study of such masters of thought as Darwin, Weismann, Galton, Delage, Féré, Naegeli, Mehnert, and Karl Pearson, I shall be happy in that I have placed him on the right road to gain a knowledge of the best that is known regarding the deep mysteries of the deeply mysterious matter of HEREDITY.[1]

Physiology of the Egg- and Sperm-Cell.

The earliest part of antenatal life is the long period during which the egg-cell and the sperm-cell are lying in the bodies of the parents of the unborn and as yet "unconceived" infant. Regarding this life's phenomena we are almost ignorant; but we know that their sum and effect are best represented by the word "heredity." We know something, it is true, of the ante-conceptional existence of the ova,—that there are thousands of them in the ovary at birth, that the number has decreased markedly at puberty, that thereafter one or two come to maturity and are expelled from their ovi-sacs once a month or thereby, that certain changes occur in the empty ovi-sac after rupture, and that a structure is formed there, called the corpus luteum, which possibly has a far-reaching effect on the nutrition and health of the whole body,—but of the early life of the sperm-cell and of the spermatozoa before they become prominent in fertilisation we know almost nothing. We may guess further that the ova as they lie in the ovary are influenced by the health or disease of the individual in whose ovaries they lie, that they in their turn may affect her life and the life and fate of the ova lying beside them, and that the corpora lutea also are not without their effect upon the physiology of the mother and of the impregnated ovum in her uterus,—we may guess these and other things about the ovum, but we have hardly begun even to guess about the spermatozoon. Yet, if we are to accept the evidences of after events, there is already in the ovum and the spermatozoon the subtle and complex machinery of heredity; in the reproductive cell, in its nucleus, in its chromosomes, or in parts of it not yet differentiated or denominated by science, there is the mysterious something which determines that the child shall resemble his parents, his grandparents, and his remoter ancestors. The individual is, as it were, the meeting-place of two long lines of spectral forms, stretching away back into the past and melting into an army of shadows, each of which in its time was a living being with habits, good or bad, with health or disease, with structures stoutly normal or defectively abnormal; the infant at birth is the living ganglion towards which many lines of influence converge and in which they meet, with effects which we cannot foretell, but about which, when we see them, we say "heredity determined them." In every human face we can read, if we have eyes and understanding, the "sequence of posterity."

> "Look here upon thy brother Geffrey's face;
> These eyes, these brows, were moulded out of his:
> This little abstract doth contain that large
> Which died in Geffrey, and the hand of time
> Shall draw this brief into as huge a volume."

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[1] The literature of *Heredity*, which is vast, will be found in the *Index Catalogue* (vol. vi. 74, 1885; 2 s., vol. vi. 1032, 1901) under *Heredity* and cross references.

It is necessary, therefore, to believe that all hereditary tendencies are already in the ovum and spermatozoon before fertilisation, for it is hardly possible to conceive of them being suddenly implanted in or conferred upon the substance of the reproductive cells at any set time, such as that of maturation. Whatever possibilities of growth, of division, of elaboration, and of differentiation, therefore, the original reproductive cells have, they also have the power in them of producing an individual closely resembling the individuals from whom they come. How the various strains of tendency are combined or antagonised or modified by such phenomena as maturation and impregnation it is hardly possible as yet to do more than surmise; but that these events do influence the future of the individual cannot, I think, be doubted. Further, the environment of the germ-cells (as we may conveniently term both the male and female reproductive elements) is not, I believe, without influence upon their future development. Thus far I have been considering solely what may be called normal or ancestral heredity, the tendency every living thing has to reproduce its like, its like but with variations, the variations constituting individuality; but it is necessary also to deal with morbid heredity, and that leads me to the discussion of the pathology of the ovum and the spermatozoon.

Pathology of the Egg- and Sperm-Cell.

Κακοῦ κόρακος κακὸν ὠόν is a Greek proverb; it may be rendered "a bad crow lays a bad egg"; and it represents the popular idea of morbid heredity. That an apparently good crow occasionally lays a bad egg, and that an undoubtedly bad crow sometimes lays a good one, are facts which are kept in the background, or explained away by a reference to an earlier ancestor of the crow tribe if they become too prominent. That is the popular view of the subject; let us, however, look at the subject from the scientific standpoint.

Heredity in relation to morbid processes is believed to show itself in various ways. Let us consider some of these.

In the first place, there exists in some families a special tendency for the members to be affected with certain maladies which manifest themselves late in postnatal life. "It may be supposed," wrote Montaigne, "that I am indebted to my father for this stonie quality, for he died exceedingly tormented with a great stone in his bladder. . . . I was borne five and twenty yeares before his sickness, and during the course of his healthy state, his third child. Where was all this while the propension or inclination to this defect, hatched? And when he was so farre from such a disease, that light part of his substance wherewith he composed me, how could it for her part beare so great an impression of it? And how so closely covered, that after fortie five yeares after, I have begun to have a feeling of it? and hitherto alone, among so many brethren and sisters, and all of one mother." The hereditary nature of renal lithiasis so graphically enunciated by Montaigne, has been affirmed for it by modern science, which has gone on to postulate a similar character for the biliary calculus, for obesity, for rheumatism, for gout, for asthma, for eczema, for migraine, and for diabetes. It is maintained, also, that what is transmitted is not so much the disease itself as the tendency to develop it; it is thought that a certain type of constitution with slow nutrition causes one or other of the above-named maladies; and there is abundant clinical evidence to prove this, as well as to show that in a certain family some of the ascendants may exhibit one of this group of diseases while the descendants may suffer from others. There may be similar heredity, or it may be of the heteromorphic kind: the gouty man has a son who becomes gouty, or he has one who suffers from hepatic calculus, from asthma, from eczema. It is even thought that after death the chemical processes of dissolution have their hereditary type, and that the tissues of the body break up in a way that has been determined for that family by remote ancestors.

In the second place, there are various nervous maladies for which a hereditary character has been claimed; from them the members of the "neuropathic family" suffer. They may be unaccompanied by structural alterations, such as various forms of insanity and epilepsy and hysteria, or they may be so accompanied, as in general paralysis, locomotor ataxia, hereditary ataxia, cerebellar ataxia, chorea, pseudo-hypertrophic paralysis, etc. There may be similar (or homologous) heredity or dissimilar (or heterologous) heredity; the maladies may show themselves at a special age and always at that age (homochronous heredity); twins may be affected with the same disease; and many minor malformations (*e.g.* hare-lip, hypospadias, microcephaly) may be associated with these nervous maladies, or may exist in the relatives of the individuals suffering from them. It is maintained that it is not always the disease itself that is transmitted, but simply a predisposition to it, a weakness of the nervous system which makes the individual prone to develop it; further, a predisposition to suffer from such maladies as gout, rheumatism, migraine, and eczema which indicate slowness of nutrition may coexist with it.

In the third place, there is the heredity of cancer and other tumours, such as uterine myomata. This also must be looked upon as a heredity of predisposition. It is not admitted by all as a real thing, and it is true that it would seem sometimes to be dependent on other factors than heredity; but I believe in the tendency to a "habit of growth" in cells, so well described and elaborated by Adami (*Brit. Med. Journ.*, i. for 1901, p. 621). What makes the tumour is the assumption by its primary cells of the habit of growth instead of the habit of work, and according to the extent of this replacement arise the various grades of tumour formation, from the most benign to the most malignant. I have elsewhere (*Brit. Med. Journ.*, i. for 1901, p. 657) pointed out that the fœtus itself is at one time in its life (about the fourth month) a most remarkable tumour, quadrupling its weight in a month; yet this rapidity of growth is checked, and differentiation of structure and functional activities take its place. If we could discover the cause which checks its growth, might we not be near the discovery of how the growth of a malignant tumour might also be arrested? At any rate I think there is abundant evidence that the tendency to a "habit of growth" may be hereditarily transmitted from ascendants to descendants.

In the fourth place, there are several diseases a predisposition to which is occasionally transmitted hereditarily, among which may be named heart disease, bronchitis, nephritis, and certain eye diseases, such as strabismus and cataract.

Now, before I proceed further in this review of morbid heredity and its manifestations, let me summarise what has been said, and draw from it a deduction or two. In all the transmitted conditions to which reference has been made (arthritic troubles, nervous diseases, neoplasms, etc.), we have been dealing with the transference from ascendants to descendants of *predispositions* or *tendencies*; we have not stated a belief in the transmission of any structural characters underlying these, and have left it to be imagined that none such existed. But it is a very open question whether such structural causes for the predispositions do not, after all, exist. If we take one or two other hereditarily transmitted diseases, such as hæmophilia, chlorosis, some forms of cataract, and the like, we know that in them there is generally believed to exist a structural substratum, such as fragility of the walls of the blood vessels, and narrowness of the arteries, which explains how this predisposition is brought about. There are, in other words, states intermediate between those in which no structural alteration is recognisable (gout, cancer) and those in which definite and specific changes can be seen (syphilis); these connecting links lead us to ask the question whether in all hereditary maladies there may not be a subtle substratum of tissue-defect which acts as the vehicle for the manifestation of the functional disorders which constitute the diseases. May there not, for instance, be a congenital narrowness of the renal arteries which predisposes in certain families to Bright's disease? Do not, therefore, these two groups of hereditary states merge into each other by an intermediate series of types? Do not the same rules apply to hereditary maladies in which there are underlying structural alterations which are transmitted and to those in which none have as yet been seen? But I must return to the main argument.

In the fifth place, there are the microbic disorders. Tuberculosis is constantly spoken of as transmitted hereditarily, but it may be meant in two different senses. In the ordinary sense it is assumed that the children of the phthisical are born with tissues which do not easily resist the onslaught of the tubercle bacillus on the attainment of a certain age and under certain conditions. There is the transmission of a predisposition. But, as I have shown in the first volume of this Manual (p. 207), there are some undoubted instances in which a tubercular mother transmitted tuberculosis directly to her fœtus; the cases are rare, and there are reasons for their rarity, but they are real. In tuberculosis, therefore, there is the possibility of the transmission of a predisposition to the disease or of the disease itself. Does this not prove that it is impossible to shut off one group of transmitted morbid states from another, or to say "these are fœtal infections, the others are hereditary transmissions"? Is there, after all, any fundamental difference between the transmission of the germ of disease and the transmission of the liability to be attacked by the germ? Smallpox, scarlet fever, measles, malaria, and many other maladies may be transmitted directly from mother to fœtus; may there not also be a transmission of the liability to be attacked by them in postnatal life? In some families there is a special proneness to be affected by one of the exanthemata rather than by another; in other families there is a certain immunity against certain diseases. I do not think we can shut off the diseases which are transmitted through the placenta to the fœtus from the maladies which are hereditarily predisposed to in antenatal life and which develop (under favourable circumstances) after birth.

In support of the preceding statement, it may be noted that many fœtal diseases agree with recognised hereditary postnatal disorders in their obedience to the laws of morbid heredity. They may show similar or dissimilar heredity; they may exhibit family prevalence; they may affect only one sex; they may be present in the children of a woman by her first but not in those by her second husband; and so on. Many references to and illustrations of these characters will be found in the first volume of this work under fœtal ichthyosis, fœtal dropsy, fœtal rickets, and the like.

In the sixth place, there is heredity among the teratological formations. The malformations and monstrosities of the embryo may, like the diseases of the fœtus, be transmitted hereditarily. Direct heredity is often prevented by the fact that so many monstrosities do not permit of postnatal life; but there are sufficient instances of it among the minor malformations, such as polydactyly, hare-lip, ocular anomalies, aural deformities, and herniæ, to prove that it undoubtedly exists. Family prevalence is comparatively frequent, and indirect heredity is common. A most striking instance of the combination of direct and indirect heredity was reported by me some years ago (*Amer. Journ. Obstet.*, xli. 577, 1900): in three generations there were defects of the thumbs; but in the third generation these suddenly became grave in character and were associated with hydrocephalus, anencephaly, absence of the radius, and spina bifida. Further, experimental teratogenesis has shown that malformations and monstrosities may be produced by acting on the embryo with the agents (toxic, microbic) which produce the diseases of the adult, the child, and the fœtus. There is not, therefore, as great a difference as might at first be imagined between the heredity of diseases and of malformations. Each group has its limitations in certain directions, but there are many characters possessed in common.

In the seventh place, and finally, there is evidence of heredity in regard to morbid conditions which are generally supposed to arise in the germinal period of life. Germinal pathology falls under the laws of morbid heredity. Twin pregnancies and large families (prolificacy) are often distinctly hereditary; the hydatid mole may occur several times in the same patient; sex anomalies may show family prevalence.

Further, I believe, it is precisely in the early part of the germinal period that predispositions and tendencies to disease and malformation are developed, and, as we have seen, they are often hereditarily transmitted. Possibly, also, it is during this early epoch that tumours are originated. I have accepted Adami's suggestion that they are due to a "habit of growth," but that does not prevent me believing also that this habit of growth was acquired in the germinal period of life. Indeed, if we imagine an arrest of the evolution of the germ at the stage of rapid growth we have a temporary condition becoming permanent; the habit of growth, instead of being checked, may continue in a few cells and so lead to the formation of a neoplasm. It is, of course, difficult to realise how it may remain latent for years, as in cancer, but I believe that in some way it does so lie quiescent until the checking force is removed and there is, again, an outburst of growth-energy. Possibly some gland, like the thymus, may check exuberant cellular growth at first; possibly the commencement of reproductive life may check it later, or turn its energies in another direction; but after active reproduction has ceased, cellular growth of an irregular uncontrolled kind may return, and a malignant neoplasm result.

I may here refer very briefly to *telegony*. This phenomenon may be defined as "the alleged influence of a previous sire on the progeny produced by a subsequent one from the same mother." That it occurs has been fairly well established both for plants (when it is termed *xenia*) and for animals and perhaps also for the human subject. The reader will find a good description of its phenomena in Brunton Blaikie's article in *Teratologia*, vol. ii. p. 157, 1895. It is possibly to be explained by the passage of small pieces of the fœtal membranes and placenta (*e.g.* syncytial fragments) into the circulation of the mother, from whom again they find their way to the ova in her ovaries and impress upon these certain characters reminiscent of the male parent. Even this theory does not explain away all the difficulties in connection with it; and I may call it again as I named it before (Vol. I. p. 185), "the wireless telegraphy of antenatal life."

Such is a brief sketch of the phenomena of morbid heredity as they are usually understood. It is to be observed that they differ in many respects from those of normal heredity. For instance, direct heredity is rare and indirect is very common; examples of family prevalence abound; the individual inherits tendencies and predispositions to various abnormal states, and he may, for instance, have one morbid state, his father another, and a brother a third. Groups of diseases are transmitted rather than single maladies, and these may apparently make an interchange with or occur along with other hereditary morbid states of another kind, such as malformations, fœtal diseases, tumours, twin-bearing, and insanity. In all these particulars morbid heredity differs from normal heredity.

I do not intend to discuss in detail the mechanism of morbid heredity; but I may indicate very simply, and without the adoption of any of the scientific nomenclatures now in vogue, how it may be supposed to arise and what it really is. I think it cannot be doubted that, during the life of the egg-cell and the sperm-cell as individual cellular elements in the body, corporeal conditions are influential in impressing upon them characters which manifest themselves later in disturbances of development, of growth, and of health. In this way two specialised cells are produced (the ovum and the spermatozoon), each of which has, in addition to its normal heredity or the hereditary tendencies of its germ-plasm, the tendencies which have been impressed upon it by morbid conditions existing in the body of the organism of which it has formed a part. In each cell there are two streams of tendency which are to influence the future fate of the new being which is to be formed from the coalescence of two of these cells. In each there is normal heredity (or simple *heredity*) which consists in the tendency to develop an organism resembling that of the typical ancestor, and morbid heredity (or, better, *non-heredity* or *degeneration*) which consists in the tendency to lose some of the energy of development present in the typical ancestor. The former tendency is always inherited, and it may be regarded as constantly associated with the germ-plasm, although it is unnecessary for a simple conception of it to introduce this idea; whereas the latter is commonly acquired in the germinal period of life, although it may also be taken on to a small extent in the embryonic and fœtal epochs, and may be handed down from one generation to another for a number of times, many or few, as surrounding circumstances determine. It is generally spoken of as morbid heredity; but it is more correct to regard it as a dissolution or breaking of heredity, as a process in which inheritance is an incident not a requisite, as an arrest in the processes of the impressing of normal tendencies upon the germ, of the ontogenesis of the embryo, of the physiological life of the fœtus, and of the health of the organism after birth. It is as if the fingers of the clock cease for some minutes to advance; the works go on but in a laboured fashion; then perhaps the cause of arrest is removed and the fingers move forward again and the mechanism once again works freely; but at the end of the hour or the day the clock is found to be slow, it has lost something which it does not regain, it has fallen behind other clocks.

But, now, there is another factor in the germinal life of each individual which requires to be referred to: there is the occurrence of impregnation of the ovum with its heredity and its non-heredity or degeneration, by the spermatozoon with its heredity and its non-heredity or degeneration. If it were not for this phenomenon the new being would be simply the old being influenced in his characters by the conditions acting upon the old during his lifetime, he would represent the sum-total of his heredity with the modifications (or arrests) imposed upon it by his environment. But sexual reproduction occurs, there is a mixing of the heredities and the acquired degenerations of *two* cells, and so the new being obtains his own individuality and is something different from each of his parents although resembling them both. This occurrence profoundly complicates the results of the combined action of heredity and acquired tendencies; it is not at the present time possible to predict the effect of the union of two reproductive cells, each of which has a tendency to health or to disease, and it is doubtful whether it will ever be possible to do more than make the most provisional of prognoses on the matter. It is possible that in some cases the healthy sperm-cell may check the degeneration going on in the morbid ovum, and *vice versâ*; but it is also possible that this may not result; and I doubt if higher mathematics can even state the problem for us, of such extraordinary complexity is it. One thing, however, seems to me to be clear—the question whether normal heredity or the abnormal breaking of heredity (degeneracy) is to predominate in any case, is largely determined during the years when the sperm and ovum are parts of the bodies of the parents.

Let us now consider whether pathological processes, causes, and effects in the various periods of life can be brought under the same laws. In the first part of germinal life, morbid causes are chiefly effective in producing tendencies which may afterwards become monstrous developments or non-developments or diseases. In the later part of germinal life, these tendencies are doubtless still being produced, but in addition there are other occurrences taking place, such as the production or determination of twins and of double terata, of teratomata, and perhaps also of some other neoplasms. In the embryonic period the action of morbid causes is producing monstrosities, malformations, and anomalies of growth; while in the fœtal period the results are diseases, but diseases with special characters, due to the peculiarities of fœtal life. After birth, as we know, morbid causes produce well-known diseases with their well-known characters. In all these periods of life, I think we can recognise that morbid causes act in much the same way, and can conclude that that way is by arresting normal processes of growth, development, and functional activity. It is easy to understand how the arrest of part of the architectural elaboration of the embryonic body produces a monstrosity; in the chapters that form the main bulk of this volume such arrested developments have been over and over again referred to and their mechanism described. Similarly, in the fœtal epoch of antenatal life, the arrested performance of physiological functions will weaken the antenatal defences (placental and other) of the unborn infant, and allow the invasion of his body by microbes or their toxines or by toxic products; the fœtal diseases result. In the germinal period the principle of arrest is not so easily grasped, but it is, to my mind, equally real. If the function of the reproductive cell before impregnation be to carry forward to the next generation the normal heredity of structure and function of the past, then it can be seen that arrest at this time means the possibility of surrounding influences interfering with this transmission; there is a break in the handing-on process, some links are wanting from the chain of health, and the future individual has points of weakness in his heredity. Again, there comes a time when maturation takes place or ought to take place; if arrestment occur here it will take the form of incomplete maturation; one polar globule alone may be expelled, not two; and so in some way, which we do not now know, the future life of the cell is interfered with. Imperfect maturation may take from the reproductive cell the power of normal fertilisation, or it may alter in some way the phenomena which follow it. Again, when a spermatozoon penetrates an ovum, some subtle mechanical or chemical change takes place whereby no other spermatozoon gains entrance; but if this mechanical or chemical change be arrested or delayed, another sperm may make its way in and monochorionic twins or a double monster may result. Similarly in the other forms of excessive development, an arrest, paradoxical as it may sound, may be the cause. Again, in the stage of the morula mass there comes a time when continuous cell-division gives place to cell-differentiation, when there is no longer simple multiplication of cells, but when one cell begins to be recognisably unlike its neighbour; if, now, an arrest occurs, the tendency will be for the cells to go on multiplying without their forming the blastocyst with all its different parts and more especially the embryo; the continuous cell division will be the result of the arrest of the specialisation of function in the massed cells. Perhaps, in this way, the hydatid mole takes origin; perhaps in this way the rudiment of the future cancer is implanted in the tissues, a cell possessing the power of indefinitely multiplying its like, but bereft of the faculty of varying the appearances and functions of its daughter cells. Other examples might be given, but enough has been said to show how this principle of partial arrest may run through the whole series of the morbid phenomena of life. Complete arrest will, of course, cause death at any of the stages of antenatal existence.

Let us now see whether we can make any generalisations regarding the causes or cause of this process of arrested growth, development, and functional activity. In the etiology of the morbid states which supervene after birth we recognise mechanical and physical traumatism, toxic agencies, microbes and their toxines, and parasites as the chief factors, along with the predispositions to contain maladies or the malformations and maladies which have existed before birth. These causes account for the pathological developments of postnatal life. When we studied the maladies of fœtal life (*vide* Vol. I. of this Manual) we found the same causes in action with certain limitations, and with variations in the results due to the intrauterine environment of the fœtus and some other circumstances. The causes of fœtal diseases were not dissimilar to these of postnatal maladies. The pathological manifestations of embryonic life have been found to be monstrosities and malformations. Now, the results of experimental teratogenesis have shown that the toxic and pathogenic agencies of postnatal life (alcohol, microbes, their toxines, etc.) produce monstrosities and defective developments when acting on the embryo; further, evidence is being gradually accumulated that malformations and monstrosities occur very frequently in the descendants of the men and women who suffer from such maladies as syphilis and tuberculosis, or who indulge to excess in alcohol, cocaine, morphia, and the like. It is more than likely, therefore, that once more the causes of the morbid states are not dissimilar but similar, and that the monstrosities and malformations of the embryo are due to no special causes but to the same toxic, toxinic, microbic, and traumatic agencies as exist in fœtal and postnatal life. The results are widely different, for the causes act upon an organism forming, not upon one already formed, and so malformations rather than diseases are the consequence. Finally, we may carry the same argument back to the germinal period of life. I believe that in this, just as in the fœtal and embryonic epochs, there are in action the same kinds of morbid causes, microbes, poisons, toxines, traumatisms; but again the results are peculiar, being alterations, by arrest, of the physiological conditions of the period. In this way twin-bearing, sterility, hydatid moles, double terata, anomalies of the fœtal annexa, tumours, and degenerative tendencies are linked on to monstrosities, malformations, and fœtal diseases as results of similar and not of dissimilar causes. It seems to me that there is abundant support for the view, that the ultimate causes of all morbid processes, antenatal and postnatal, are essentially the same in their nature, while their results differ widely because of differences in the structure and physiology of the organism at the time when they come into action. There is an etiological similarity or uniformity, therefore, in the various stages of life. The wall of division which has separated antenatal from postnatal pathology is thus broken down; can it be doubted that the result will be a greater and a clearer knowledge of the peculiarities and characters of the morbid processes of both periods of life?

Treatment of Antenatal Morbid States.

I have already, in the closing pages of the first volume of this work (pp. 451–487), indicated how antenatal morbid states, and more especially fœtal diseases, may be treated with a view to their prevention or cure, and I shall not repeat here what was written there;[1] but I may add a few conclusions which seem to me to follow from the consideration of the special matters dealt with in this volume.

It has been shown, for instance, that embryonic monstrosities and malformations sometimes show a tendency towards repair during the fœtal period of antenatal life (*vide* spina bifida, hare-lip, etc.); it has also been demonstrated that, even in the family with most malformations and monstrosities, some members come into the world free from morbid states (*e.g.* the offspring of the monstriparous woman described in the *American Journal of Obstetrics*, xli. 577, 1900); and it has been suggested that morbid heredity is rather a break in the heredity of health and normal formation which may be mended again if not perhaps in one generation, at any rate in two or three. These phenomena show, at least so it seems to me, that there is a constant tendency towards recovery and the return to a healthy stock. The practical conclusion as to therapeutics is, therefore, to try to secure that the specialised reproductive cells which are to become the infants of the next and of succeeding generations be preserved from the impact of morbid agencies (toxic, microbic, toxinic, traumatic) so long as they are in the bodies of the men and women of this generation. Let me expand this idea a little.

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[1] But it will greatly help the reader if he will re-read these pages now.

It is obvious that if a man or a woman has a body poisoned with the septic products of smallpox, infected with the toxines of tuberculosis or syphilis, or irrigated with fluids containing morphia, lead, cocaine, or (most of all) alcohol, his and her reproductive cells cannot escape the morbid influence thus brought to bear upon all the other tissues. We know that certain poisons specially affect certain tissues (*e.g.* lead, the nervous system), and possibly others specially affect the reproductive cells; but these peculiarities do not influence the argument, they only serve to explain the diversities of the results. There is reason to believe that reproductive cells so surrounded by malign influences grow into malformed embryos, diseased fœtuses, and infants predisposed to various maladies; in other words, the chain of normal heredity is broken in them, and morbid heredity or degeneration takes its place. But the individual in whose body these reproductive cells lie may recover from the illness from which he or she is suffering (*e.g.* typhoid fever, tuberculosis, syphilis), or may cease to supply his other tissues with noxious drugs, narcotic or alcoholic; under these circumstances there is evidence to show that the reproductive cells may join in the general tissue recovery and convalescence which sets in. A drunkard's nerve cells may seem to be hopelessly enfeebled, and yet total abstinence may wonderfully recover to him a mental vigour which had seemed as if lost for ever; is it not possible that it may do as much for the reproductive cells? But, it is said, his reproductive cells have already been weakened by the excesses of his father before him; they are predestined to be easy victims to morbid influences. There is the predestination of morbid heredity. True, but there is also the initiative of individual effort to be taken into account. "I am I, howe'er I was begot." In one generation much may be done to restore the germ-plasm or the substance of the reproductive cell to a healthy state, for I conceive that its true heredity ever impels it in that direction. It is a family matter, is this kind of treatment. The cleanness of life and the control of the indulgence of morbid cravings for narcotics and stimulants of the parents does much, but it may be insufficient to effect a cure; the children may, so to say, have to continue the treatment for the benefit of their children, and so on, possibly, for one or two generations. Family diseases require family treatment. Further, during the process, it will be well that marriages of consanguinity be avoided, and that each individual shall not postpone matrimony till late in life ("opsigamy") or embark upon it at too early an age (*e.g.* before nubility). It need hardly be said that it will likewise be well for the individual, against whom "from his cradle fate and his fathers fight," to make no matrimonial alliance with one endowed with the sad legacy of family ill-health, unless indeed she also is making a good struggle to redeem for her germ-cells some measure of health and strength. Eugenesis or well-begetting is one of the world's most pressing problems—it is far from being a hopeless one, but it must be attempted before it can be solved.

APPENDIX

List of Names of Medical Men who have supplied me with Specimens or Records (generally with Photographs) of Cases of Antenatal Disease or Malformation, or who have enabled me to examine Patients suffering from Congenital Anomalies. Of Specimens there have been 206, of Patients 54, and of Reports 170, making a total (including my own observations in Private and Hospital Practice) of 500. The numbers within brackets simply refer to my List in my Case Books.

Amner, Mr. F. H., Edinburgh. *Specimen* of Stillborn Twin (16).

Andrews, Dr. H. R., London. *Report* on case of Congenital Prolapsus Uteri (441).

Annandale, Prof., Edinburgh. *Patient* with Congenital Defect of Perineum (241).

Anonymous, Grimsby. *Specimen* of Iniencephaly (277).

Anonymous. *Report* on Pygopagous Twins (471).

Ashby, Dr. H., Manchester. *Report* on case of Fœtal Nephritis (447).

Baildon, Dr., Southport. *Specimen* of Meningocele (34).

Ballantyne, Dr. A., Eskbank. *Specimens* of Encephalocele (22), Gastroschisis and Anencephalus (24, 178).

Ballantyne, Dr. H. S., Eskbank. *Specimen* of Hydrocephalus (235).

Barbour, Dr. A. H. F., Edinburgh. *Specimen* of Fœtal Anasarca and Obesity (11). *Patient* with Anomaly of Hairy Scalp (305).

Barnardo, Dr. G. F., London. *Report* on cases of Ectopia Cordis (390) and Hypospadias and Uterine Malformation (426).

Bell, Dr. Joseph, Edinburgh. *Patient* with Imperforate Anus and Double Vagina (201).

Beveridge, Dr., Leith. *Specimen* of Fœtal Dropsy (218).

Bidone, Dr. E., Florence. *Report* of Fœtal Endocarditis (474).

Blackwell, Dr. E., Hastings. *Report* on case of Spina Bifida (433).

Bluck, Dr. Cardy, London. *Specimen* of Congenital Hydronephrosis (140). *Report* on two cases of Anencephalus (364, 365), two of Fœtal Dropsy (366, 367), one of Fœtal Ascites (368), one of Duodenal Atresia (369), one of Absence of Radius (370), and one of Anchyloses (371).

Booth, Dr. M., Edinburgh. *Specimen* of Twin Abortion Sac (236).

Boxer, Dr. E. A., Edinburgh. *Specimen* of Fœtal Death (244).

Brayton, Dr. A. W., Indiana, U.S.A. *Report* on Thoracopagous Twins (384).

Brewis, Dr. N. T., Edinburgh. *Specimen* of Deformed Extrauterine Fœtus (35).

Brook, Dr. W. H. B., Lincoln. *Report* on two cases of Congenital Hæmophilia (444, 445).

Brooke, Dr. W. F., Swansea. *Report* on Congenital Obstruction of Intestine (363).

Brown, Dr., Hanley. *Specimen* of Gastroschisis (23).

Brown, Dr. E. E., Inverness. *Report* on Meningocele (468).

Buist, Dr. R. C., Dundee. *Reports* of specimen of Fœtus Papyraceus (374), Congenital Teeth (387), Hydrocephalus and Cervical Spina Bifida (397).

Bunting, Dr., Edinburgh. *Patient* with Unilateral Anophthalmus (240). *Report* on Congenital Amputation of Digits (436).

Butchart, Dr. C. A., Leith. *Specimen* of Fœtus with Multiple Deformities, including Spina Bifida (113).

Caird, Mr., Edinburgh. *Patient* with Polydactyly (138).

Cairns, Dr. Murray, Liverpool. *Specimen* of Iniencephaly (252).

Calder, Dr., Leith. *Specimen* of Cystic Kidney and Hypospadias (327).

Callender, Dr. T. M., Edinburgh. *Report* on Fœtal Dropsy (428).

Calwell, Dr., Wellington. *Specimen* of Anencephalus (172).

Cappie, Dr. James, Edinburgh. *Specimen* of Anencephalus (194).

Carmichael, Dr. E., Edinburgh. *Specimen* of Fœtal Ascites and Distended Bladder (197).

Carmichael, Dr. James, Edinburgh. *Specimens* of Deadborn Fœtus (107, 125).

Charles, Dr. E., Indiana, U.S.A. *Report* on cases of Encephalocele (425), of Anencephalus (449).

Chiarleone, Dr., Catania. *Report* on specimen of Fœtus Amorphus Anideus (360).

Chiene, Prof. J., Edinburgh. *Patient* with Ectrodactyly (292).

Clarkson, Dr. R. D., Falkirk. *Specimen* of Anencephalus with Placenta (278).

Cordes, Dr. L., New York. *Report* on case of Fœtal Ichthyosis (498).

Cormack, Dr. W. P., Dudley. *Report* on cases of Polydactyly (453) and Epispadias (459).

Cotterill, Mr. J. M., Edinburgh. *Patient* with Double Labial Fistula (221).

Croom, Sir Halliday, Edinburgh. *Specimen* of Fœtal Dropsy (102).

Darling, Dr. T. B., Edinburgh. *Specimens* of Atresia Ani and Club-Hands (21), Fœtal Measles (52), Stillborn Infant (80), Deadborn Infant (123, 131, 171). *Patients* with Congenital Amputation (41), Occipital Encephalocele (304). *Report* on Congenital Singultus (389).

Davidson, Dr. S., Penrith. *Specimen* of Fœtal Chondrodystrophia (101). *Report* of case of Polydactyly (77).

Dendle, Dr. F., Lochgelly. *Specimen* of Anencephalus (169).

Dickson, Dr. D. E., Lochgelly. *Specimen* of Fœtal Death (301). *Report* on Facial Paralysis in Newborn Infant (429).

Dickson, Dr. G. A., South Queensferry. *Specimen* of Pseudencephalus (309).

Doherty, Dr., Chicago. *Report* on case of Intrauterine Fracture (435).

Doran, Dr. A., London. *Report* on Cystic Ovary in Fœtus (349).

Drysdale, Dr., Edinburgh. *Specimen* of Kitten with Absence of Fore Limb (195).

Dumesnil, Dr. Ohmann, St. Louis, U.S.A. *Reports* on Fœtus Amorphus Mylacephalus (383), Hairy Nævus (412).

Dwight, Dr. T., Boston, U.S.A. *Report* on case of Double Hand (353).

Easby, Dr., Peterborough. *Report* on Antenatal Fracture of Clavicle (396).

Edmondson, Dr. J., St. Helens. *Specimen* of Paracephalic Twin (30).

Elder, Dr. G., Leith. *Patients* with Congenital Tylosis Palmæ et Plantæ (164), Hemiatrophy of Face and Malformed Ear (181). *Reports* on Vulvar Anus (399), Congenital Fragility of Bones (430), and Oligodactyly (431).

Elder, Dr. W., Edinburgh. *Specimen* of Iniencephaly (44).

Evans, Dr. J. H., London. *Report* on case of Cervical Auricle (466).

Falconer, Dr. J. F., Edinburgh. *Report* on Twins with Erysipelas Neonatorum (418).

Farncombe, Dr. W. T., Harborne, Birmingham. *Report* on case of Congenital Heart Disease (439).

Farquharson, Dr. J. M., Edinburgh. *Specimen* of Stillborn Fœtus and Placenta (132).

Farquharson, Dr., Newcastle. *Specimen* of Anencephalus, etc. (155).

Felkin, Dr. R., London. *Patient* with Vascular Nævus (75). *Report* on various cases of Maternal Impression (339–345), Congenital Contraction of Fingers (357).

Ferguson, Dr. R. T., Anstruther. *Specimen* of Anencephalus (222). *Report* on Anencephalus (470).

Fleming, Dr. R. A., Edinburgh. *Specimen* of Imperforate Anus (248).

Fordyce, Dr. W., Edinburgh. *Specimens* of Hernia of Umbilical Cord (39), Iniencephaly (251). *Report* of case of Fœtal Ascites (473).

Fowler, Dr. J. S., Edinburgh. *Patient* with Hemi-Hypertrophy (224). *Specimen* of Placenta and Cord (291). *Report* on Antenatal Convulsions (440).

Freeland, Dr., Broxburn. *Specimens* of Fœtal Dropsy (9, 10) and Anencephalus (226).

Geddes, Dr. A. M. C., London. *Report* of Placenta with Tumour (417).

Giles, Dr. A., London. *Report* on Fœtus with Distended Bladder and Absence of Urethra (386).

Glegg, Dr., Edinburgh. *Specimen* of Anencephalus (279).

Goudie, Dr., South Shields. *Specimen* of Anencephalus (135).

Govan, Dr. G., Cockermouth. *Specimen* of Iniencephaly (320).

Gradwohl, Dr. R. B. H., St Louis, U.S.A. *Report* on case of Fœtal Cerebro-Spinal Meningitis (434).

Graham, Dr. F. M., Edinburgh. *Specimens* of Placenta from Hydramnios (116), Lobulation of Kidney (128), and Congenital Diaphragmatic Hernia (166). *Patients* with Vestibular Cyst (127), Encephalocele (143).

Grant, Dr. Taylor, Edinburgh. *Specimen* of Battledore Placenta (303).

Green, Dr. J. L., Edinburgh. *Specimen* of Hydrocephalus (286).

Gulland, Dr. G. L., Edinburgh. *Specimen* of Abortion Sac (106).

Günsburg, Dr. M., Charkow, Russia. *Report* of Fœtal Ascites (402), Quadruplets (499), and Spina Bifida (500).

Guthrie, Dr. Cowan. *Specimen* of Dermoid Cyst or Pseudo-acormus (33).

Harris, Dr. R. P., Philadelphia. *Report* on two cases of Absence of Penis (413, 414).

Hart, Dr. D. Berry, Edinburgh. *Specimens* of Embryonic Gastroschisis (65, 66), Anencephalus (122), Hydrocephalus (151), Anencephalus (206). *Patient* with Polymastia (149).

Harvey, Dr., Edinburgh. *Specimen* of Anencephalus (168).

Haultain, Dr. F. W. N., Edinburgh. *Specimen* of Achondroplasia (273).

Hellier, Dr. G. B., Leeds. *Report* on two cases of Elephantiasis Congenita Cystica (455, 456) and on Malformed Cranium (493).

Helm, Dr. J., Edinburgh. *Specimens* of Abortion Sacs (42, 64, 70).

Helme, Dr. A. T., Manchester. *Specimen* of Phocomelus (15).

Henderson, Dr. E., Kirkcaldy. *Cases* of Premature Infant (307), Postmature Infant (308).

Henderson, Dr. E. R., Hull. *Report* on case of Hernia of Umbilical Cord (461).

Hinsdale, Dr., Philadelphia. *Report* on case of Pseudo-hermaphroditism (362).

Hughes, Dr. H. L., Dowlais, Wales. *Specimen* of Dimidiate Placenta (332).

Hutchinson, Dr. J., London. *Report* on cases of Absence of Pectoral Muscles (437), Double Penis (438).

Hutchison, Dr. R., London. *Specimen* of Fœtal Dropsy (104).

Hutton, Dr., Edinburgh. *Specimen* of Constriction of Duodenum (190).

James, Dr. Alexander, Edinburgh. *Patients* with Hereditary Syndactyly (202), Vaginal Atresia and Cervical Ribs (227).

Jamieson, Dr. W. Allan, Edinburgh. *Patient* with Tylosis Palmæ (217).

Jennings, Dr. D. D., New York. *Report* on case of Congenital Cranial Depressions (356).

Jones, Dr. B., Leigh, Lancashire. *Report* of case of Fœtal Rigor Mortis (375).

Jones, Dr. Howard, Newport, Wales. *Specimen* of Sympodia (250).

Kennedy, Dr. C., Edinburgh. *Specimen* of Postmature Anencephalic Fœtus (258).

Ker, Dr. C. B., Edinburgh. *Specimen* of Gastroschisis (124).

Kynoch, Prof. J. A. C., Dundee. *Report* on cases of Coiling of Cord (361), Dwarf Embryo (379), Stenosis of Bile Duct (380).

Lackie, Dr. J. Lamond, Edinburgh. *Specimen* of Double Chicken (242).

Landsborough, Dr. D., Changhoa, Formosa. *Report* on three cases of Transposition of Viscera (419, 420, 421).

Langwill, Dr. G., Leith. *Specimen* of Encephalocele (193).

Lawson, Dr. T., Edinburgh. *Specimen* of Hernia of Umbilical Cord (27). *Patient* with Deformity of Penis (79).

Loeb, Dr. A. H., Montreal, Canada. *Report* on Chick with Four Legs (416).

Lundie, Dr. R. A., Edinburgh. *Specimens* of Hydrocephalus and Absence of Thumb (71), Anencephalus and Deformed Thumbs (148), Dead Fœtus and Placental Hæmorrhage (165), Fœtus Papyraceus (209), Dead Fœtus and Placenta (238), Fœtus with Absence of Radii, etc. (245), Knot on Cord (253), Dead Fœtus and Placenta (257), Diseased Placenta (275). *Patient* with Desquamation of Cuticle (213). *Report* on two cases of Defective Thumb Muscles (354, 355).

Macgregor, Dr., Jedburgh. *Specimens* of Anencephalus (232), Abortion Sac (262).

Mackenzie, Dr. R., Montreal, Canada. *Report* on case of Fœtus Amorphus Anideus (454).

Mackness, Dr. G. O. C., Broughty-Ferry. *Report* on case of Macrodactyly (442).

Maclagan, Dr., Sleaford, Lincolnshire. *Specimen* of Gastroschisis (268).

MacVicar, Dr., Dundee. *Report* of Congenital Prolapsus Uteri (398).

Macvie, Dr. S., Chirnside. *Report* on Fœtal Death (448).

M'Bride, Dr. P., Edinburgh. *Patient* with Dermoid on Nose (263).

M'Elney, Dr. E., Birmingham. *Report* on case of Hypoagnathus (443).

M'Gregor, Dr. R., Hull. *Report* on case of Fœtal Death (464).

Male, Dr. H. C., Essex. *Specimen* of the Fœtus Papyraceus (103). *Report* of Congenital Intestinal (Duodenal) Atresia (338).

Mann, Dr. F. W., Ashton-under-Lyne. *Specimen* of Fœtal Dropsy (54).

Martin, Dr. A. A., North Shields. *Specimen* of Encephalocele (26).

Martin, Dr. Charles, Birmingham. *Report* on Anencephalic Postmature Fœtus (382).

Martin, Dr. J. W., Leith. *Specimen* of Hydatid Mole (46).

Martine, Dr. W. R., Haddington. *Report* on Congenital Teeth (394).

Menzies, Dr. D., Edinburgh. *Specimen* of Anencephalus (6).

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